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Intervention to promote physical activation and improve sleep and response feeding in infants for preventing obesity early in life, The Baby-Act Trial: Rationale and Design

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Abstract

Infant obesity is increasing in the US, particularly among Hispanics. Rapid weight gain during infancy increases the risk of obesity later in life and could be prevented through multi-modal interventions addressing multiple risk factors through population-level programs.

Objectives: 1) determine the extent to which the intervention, compared with the usual care control condition, improves healthy weight gain and specific behaviors (physical activity, sleep, diet) in the first year of life and 2) evaluate the cost of the intervention as a modification of the current WIC standard of care.

Methods: The lifestyle intervention focuses on age-appropriate infant physical activation, healthy sleep and sedentary patterns, and response feeding, by improving parenting skills delivered through a combination of technology (web-platform and text messages) and phone counseling. It is being tested among caregivers of infant participants of the Puerto Rico WIC program through a cluster-randomized controlled trial in 14 WIC clinics in San Juan starting in pregnancy until the infant is 12 months of age. The main outcome is infant rate of weight gain at 12 months; secondary outcomes include objectively measured hours of infant movement, sedentary behaviors

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and sleep, diet quality score and response feeding behaviors. We are also recording fees, time and personnel involved in the intervention development, maintenance and dissemination.

Conclusions: If successful, the intervention could be incorporated as a ‘best practice’ through WIC policy as a means to strengthen obesity prevention efforts to improve minority health and eliminate health disparities among Hispanics and possibly other at-risk groups beyond the childhood period.

Keywords

infant; obesity; Puerto Rico; WIC; intervention; web-application

Introduction

Obesity is a chronic health condition that increases the risk of hypertension, diabetes, and metabolic syndrome including within the pediatric population. Worldwide, overweight and obesity affects 41 million children under 5 years [1]. In the US, an estimated 23.7% of children 1 to 5 years of age who participate in The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) are either overweight or obese [2]. Most recently, a report from the Center for Disease Control (CDC) showed that adjusted obesity prevalence decreased from 15.9% in 2010 to 13.9% in 2016 in children 2–5 years participating in WIC [3]. Infants too are affected with an estimated 8.1% of US infants categorized as overweight or obese [4]. Infant obesity among Hispanics has a higher prevalence (14.8%) as compared to Blacks (8.7%) and Whites (8.4%), making this a significant health disparity among this racial and ethnic group [4]. In Puerto Rico, we found an even higher rate of overweight and obesity in 291 infants’ participants of a WIC clinic (20.6%) [5]. Rapid weight gain during the first year of life is a concern as it increases the risk of obesity and other chronic conditions in childhood and later in life [6–9]. This early rapid weight gain is also greater among Hispanics compared to Whites [10,11].

Establishing healthy feeding and physical activity behaviors early in life may prevent obesity later in life [12,13]. However, there are only a few interventions to date targeting the infant population, yielding mixed results [12,13]. In addition, there are only a handful of interventions to increase physical activity and improve sleep in young children [14–16]. Most trials have been underpowered, with low compliance and adherence, geared towards increasing knowledge without increasing parental skills. Another important limitation is that previous studies have generally not included Hispanics with few targeting early-life systems and public health policies. Current evidence suggests that to achieve the desired effects, trials should focus on multiple risk factors (i.e., eating behaviors, physical activity, sleep and parenting skills), and be delivered at multiple levels (individual, family, and community) using programs at the population-level in order to be translatable, cost-effective and sustainable [17].

To this end, interventions done within the WIC program provide a potentially powerful way of fostering early development of healthy behaviors which are key to avoiding obesity. The WIC program covers about 50% of all pregnant women and young children in the US (79% in Puerto Rico) [18]. Although the current WIC curriculum has improved breastfeeding

practices among their participants (31% breastfeeding in 2015), only 13% were exclusively breastfed [19]. In our studies among WIC infants and toddlers in Puerto Rico, we have shown low breastfeeding rates, early introduction of complementary foods and juices, low diet quality (particularly after 12 months of age), low compliance to sleep and physical activity and other non-healthy feeding practices [5,20,21]. Therefore, this program needs complementary approaches using technology to continue improving feeding practices as well as including other components that have been shown to be important for preventing obesity.

Therefore, we designed the BabyAct trial, an intervention integrating various risk obesity factors leveraging technology and using a population-level program (i.e., WIC) to facilitate translation of the intervention. The Baby-Act trial offers a structured curriculum with a combination of key messages and activities designed to promote sound parenting skills that support and sustain healthy lifestyles (i.e., developmentally appropriate exercises for 'infant activation', sleep and response feeding) beginning in the 3rd trimester of pregnancy until 12 months of age. It complements the current standard of care of the WIC Program. We will assess the clinical effectiveness of this novel complementary intervention among caregivers of infants who are participants of the Puerto Rico WIC program through a cluster-randomized controlled trial of WIC clinics located within the Extended San Juan Metropolitan Area. To our knowledge, no study has tested this type of intervention among infants. If successful, this intervention could be easily adopted as a policy-supported best practice by the WIC program to help prevent obesity among young children. This will help improve minority health and eliminate health disparities among Hispanics and other at-risk groups.

Methods

Study Design

The Baby-Act trial is a cluster-randomized controlled trial of WIC clinics in the Extended San Juan Metropolitan Area, in Puerto Rico. Clinics were randomly assigned to the intervention arm or to the control (usual care) arm. The intervention combines key messages and activities designed to promote sound parenting skills that support and sustain healthy lifestyles (i.e., developmentally appropriate exercises for 'infant activation', sleep and healthy eating behavior) beginning at the 3rd trimester of pregnancy and until the infant is 12 months of age. Participants (mothers) are currently being recruited at the WIC clinics during the last trimester of pregnancy. Mothers receive initiation modules (a total of 5) during pregnancy, to promote familiarity with the distance learning platform and readiness to initiate breastfeeding. The multimodal intervention initiates once the eligibility is confirmed following the baby's birth. The primary, intention-to-treat, analysis will evaluate the effect of the intervention on adequate infant weight gain from birth until 12 months. The intention-to-treat approach will allow us to evaluate the expected effect of adding the proposed intervention to the current WIC curriculum [22]. Secondary analyses will include effects of the intervention on objective measures of infant activation, sedentary behaviors and sleep, and feeding practices. We will also evaluate the cost of the proposed intervention as a modification of the current WIC curriculum.

Setting

This study is currently being conducted in WIC clinics in Puerto Rico, a US territory in which 98.9% of the population is Hispanic [23]. There is a total of 89 WIC clinics throughout the island; however, we chose only 14 clinics located in the Extended San Juan Metropolitan area to ensure viability of assessments by study staff in the community setting within the study period. WIC clinics were distributed be equally (1:1) to the intervention (n=7) or to the control (n=7) arm. Selection criteria of these clinics included: 1) pre-trial facility visits were performed to confirm that eligible clinics have enough space to conduct study related activities (recruit participants, conduct individual sessions, and study assessments [5 clinics were excluded due to lack of space; these clinics were not different from the other clinics in terms of the criteria for their selection]); 2) each clinic has a relatively large number of pregnant participants to recruit from (on average, there are 2,687 total participants enrolled in these clinics per month, with 222 pregnant women, 415 infants, 381 toddlers aged 12–24 months, and 1,315 children aged 2–5 years); 3) no anticipated change in clinic location or area of service; and 4) no structural damages following Hurricanes Irma and Maria in 2017. Each WIC clinic has approximately 3 nutritionists, 2 administrative staff, 1–2 assistants, and a lactation consultant. As part of the current standard of care, pregnant participants are followed 3 times during the last trimester, and they are required to attend to 3 breastfeeding classes before giving birth.

Randomization of WIC clinics

We used a random allocation process for each clinic with the exception of the 2 satellite clinics, which were randomly assigned separately to ensure assignment of 1 satellite clinic per treatment arm. This was deemed necessary as the flow of participants at these sites differs from other clinics due to extended working hours and location of facilities (shopping malls). Randomization took into account the number of pregnant participants per clinic as well as breastfeeding statistics (breastfeeding initiation and breastfeeding exclusively for 6 months) as an important determinant of future infant obesity.

Subjects/sample

We are currently recruiting pregnant women age 18 years and older who are participants of the WIC program that: 1) are in the 3rd trimester, 2) intend to enroll their infant in the WIC program when he/she is born, 3) are experiencing singleton pregnancies; 4) agree to participate independently of the assigned group; and 5) can read Spanish and have access to the internet. We are excluding pregnant women that: 1) report high risk pregnancies (history of hypertension of any type, diabetes of any type, antenatal diagnosis of intrauterine growth failure or major congenital anomalies); 2) who plan to leave their WIC clinic within the study time frame; and 3) a history of emotional or mental health disorders that would preclude active participation in the study. Also, infants born prematurely (before week 37 of gestation), with developmental disabilities, with severe conditions such as hypoxic ischemic encephalopathy, feeding disorders, intractable seizures or any other severe neurologic or muscular disorders and metabolic diseases that require specialized diet, and those requiring prolonged hospitalization at birth (>7 days) are also being excluded from participation once the diagnosis is achieved.

We are collecting information on infants who fail to meet eligibility criteria at birth as long as parents agree to complete follow up visits. This will allow us to consider the effects of our lifestyle intervention as pragmatic trial, but data collected on infants not eligible for the parent study will not be included in the assessment of the primary outcome according to study protocol.

Screening, recruitment and consent

WIC clinical staff identify eligible participants at routine prenatal visits and refer them to study recruiting staff or provide the study flyer with the contact information. We have also posted the study flyer at obstetrical offices located near or that provide services to the population associated to the WIC clinics enrolled in the study. Also, our recruiting staff identify eligible participants in the clinic waiting room. If eligible, the potential participant receives a detailed explanation of the study and we answer all their questions. If interested in participating, we confirm the remainder of eligibility criteria before moving forward with recruitment using a standardized screening form. If eligibility is confirmed, then the informed consent is conducted in a private area and we proceed immediately with the baseline visit. This baseline visit includes only self-reported questionnaires to be completed by pregnant participants (30 minutes approximately). Participants are informed by phone of their assigned group by the interventionist to maintain blindness of the assessment team. Those assigned to the intervention group receive information on how to access the web-platform, about the regular text messages that they will be receiving to reinforce the intervention and about the follow-up calls during the study.

Intervention

Theoretical basis of the intervention—The intervention is based on the Health Self-Empowerment Theory [24] and also on Bandura's Social Cognitive Theory [25]. The intervention messages are based on the self-efficacy model to increase awareness, skills, and self-efficacy. It also relies on the interaction between personal, behavioral, and environmental determinants whereas individuals gain knowledge from interaction with their environment, observing and modeling other individuals' attitudes and behaviors. We apply a multi-modal approach, in which we deliver the intervention through a web-based platform, supported by text messages and follow-up calls. The adaptation of the messages into the multi-modal approach was done using the Persuasive Technology [26] and Persuasive System Design [27] models. These models focus on the human-computer interface and how technology can/is used as a persuasive tool for behavior change.

Intervention components—Participants assigned to the intervention clinics continue to have access to and receive WIC benefits as per the current standard of care which includes nutritional education as individual and group sessions. Exposure to other platforms including distance learning (i.e., Web pages provided by the program) or other sources are being documented throughout the study.

The Baby-Act intervention includes the following components:

1. *Activation*: this curriculum was developed in collaboration with an expert on adapted physical education to ensure developmentally appropriate and safe

physical activity interactions between the infant and the caregiver. We developed professional videos showing local caregivers performing the activities recommended with their babies. These activities were geared towards increasing movement, such as playing games with their arms and legs in the first few months and activating the baby while breastfeeding, promoting tummy time and crawling in the second and third trimester of life, and promoting more movement towards the end of the first year of life. We also show ways of promoting free play (within a safe environment) and leisure time and focus on limiting sedentary activity, such as informing about the amount of time a baby should be sitting and the detrimental use of restraining movement when babies are in a car seat or baby chair.

2. *Healthy sleep patterns:* the curriculum includes recommendations on establishing adequate sleep hygiene, including the total sleep time during the day and night, how to identify early signs of sleepiness, how to swaddle their baby, how to help infants differentiate between night and day, how to promote a healthy sleep routine, to prevent using the bottle to put the baby to sleep and how to put the baby back to sleep when waking up at night without overfeeding, showing how to teach their baby to fall asleep on their own, and how to adapt babies' sleep routine as they grow.
3. *Screen time:* the developed curriculum includes recommendations on the number of hours of screen time appropriate for each developmental phase. Throughout the curriculum it is stressed that babies younger than 18 months of age should not engage in screen time, unless it is to interact with an adult. And if the parents or caregivers do allow screen time, we give them examples of recommended programs.
4. *Response feeding:* because WIC already addresses several messages in relation to breastfeeding and introduction of complementary foods, the developed curriculum focuses on other components of feeding such as identifying hunger and satiety cues, differentiating between crying for hunger and crying for other reasons, connecting response feeding with breastfeeding, showing how to pace feed if formula feeding, showing how to reduce distractions (such as TV) when feeding, showing how to practice baby-led weaning, promoting that babies 6 months and older start joining family meals, allowing infants to self-feed with a variety of healthy finger foods, showing how adding foods to the bottle can lead to overfeeding, showing ways to identify if baby is ready to stop night feedings and how to start this process, showing the transition to sippy cup at 12 months of age, discussing about avoiding using food as punishment or reward, and in general, practicing mindful eating for their baby and the entire family.

Delivery of the intervention—The intervention is being delivered using the following multi-modal approach, as soon as mothers are recruited into the study:

1. *Web-based platform:* A commercially available web-based interactive and structured instructional platform is the main delivery method for the intervention

educational content. This platform functions like an app when deployed on mobile phones and provides media-rich, communications-enabled information that has been effective for promoting healthy behaviors [28,29]. Lessons were prepared in this platform based on developmentally appropriate content to increase knowledge, skills and promote health behavior change. Participants use an assigned user code to access the platform which provides individualized measures of exposure to intervention materials and the degree of interaction with the platform. During pregnancy, there are 5 sessions that provide an overview of the program in which mothers are asked to complete before the baby is born. As soon as their infant is born, mothers receive access to the weekly lessons in groups of 4 lessons per month so that these are age appropriate. The last session ends when the baby is 12 months old. Each lesson includes assessment of acquired knowledge and willingness to incorporate behaviors presented into their daily living activities. Messages are repeated throughout the intervention but modified as the infant develops. The information is provided in an interactive way, with videos, images, questions, and input from the participants. As part of the activities, we ask participants to send audio, videos or images of participants doing activities with their babies. Also, participants are asked to establish a goal for the week, which are reviewed automatically in the web-platform the following week, with the following question “were you able to accomplish the goal set last week about xx?” for which participants answer yes or no, with appropriate motivational responses to continue their great work or to try to accomplish it during the following week. The goals are simple and could include activities such as communicating information from a lesson to a family member, performing a recommended or illustrated activity for certain number of days, or starting a new routine using information from the intervention that week.

2. *Follow-up via text messages:* participants receive automatic text messages on a weekly basis to reinforce the intervention, such as short messages on the physical activation recommendations and other healthy behaviors based on the infant’s age following the established curriculum. Participants also receive a link to the weekly lesson by text messages every week to ease the process of completing the lesson. This link takes them directly to the assigned lesson. We are using the Slicktext™ platform for this.
3. *Individual counseling by phone:* the interventionist (a PhD in Nutrition Education and registered dietitian) provides follow-up calls every three months to reinforce the intervention, evaluate the use of the web-platform and assess the adoption of the healthy behaviors as per the curriculum. Also, the interventionist reviews the data from the goal setting in the web-platform to discuss with the participant in the call, to discuss ways to improve this, if necessary. Participants have the opportunity to call in to the study interventionist if they need assistance in performing the recommended study interventions or accessing the web-platform. If needed, we schedule in-person sessions at the participant’s WIC clinic to discuss technical problems with the intervention or access to the web-platform. The lifestyle interventionist was trained to deliver all aspects of the

intervention based on the theoretical models used, as accomplished for previous studies [30]. Having a registered dietitian deliver the intervention was intended to ease the translation of the research intervention into standard practice within the WIC program, as this program is mainly run by dietitians.

Strategies to promote adherence to the intervention—Several features of the intervention design and implementation were integrated to ensure compliance is maximized. The intervention is web-based, allowing easy and constant access to all the components of the intervention. There is frequent contact between the interventionist and participants with weekly text messages and follow-up calls every three months. As part of the calls, we ask questions about the progress of the intervention, barriers to performing the behaviors shown in the lessons and ways to overcome some of these barriers. We promote strong connections with the study “brand” to maximize compliance. Also, we encourage the involvement of family members (i.e., infant father, grandparents, aunts and uncles) in the intervention activities. Acknowledgement of efforts and contributions by significant others are provided to maintain engagement and it is being recorded.

Assessment of adherence, fidelity, and level of participants’ responsiveness—Adherence to the intervention will be assessed by reviewing the data analytics from the web-based platform on the number of lessons completed by participants, responses to questions asked, and the level of compliance to the goal settings (self-reported by participant in the next lesson). Adherence is also assessed by reviewing in the phone call if they are reading the SMS and by the number of calls completed with the interventionist.

Fidelity to the intervention will be assessed by reviewing data analytics from the web-based platform in relation to the completion of lessons in the intended order, by reviewing if the SMS were automatically sent and received in Slicktext and by reviewing if the calls were completed in order and if all the components of the call were discussed.

The level of participants’ responsiveness (engagement of the participants) will be assessed by the number of goals met by each participant, by the number of pictures or videos uploaded (when the lesson asks for these), responds to SMS in Slicktext), and by reviewing the following in the calls: by explaining how SMS were helpful, by explaining how she is overcoming barriers for completing goals, by mentioning successes/difficulties regarding intervention-related behaviors (swaddling, playing with baby, no screen time, regular napping, etc.), and by identifying elements of the intervention that were not helpful and why.

Control (usual care) group

Participants recruited in randomly assigned control clinics receive the WIC program standard of care. This includes the standardized infant’s WIC certification visit a 0–1 months and re-certification visits at 6 and 12 months. Also, it includes two educational contacts every 6 months; these can be done in person or through the WIC educational web page. We will document their involvement and compliance to the standard of care provided in WIC.

Main outcomes

All outcomes are evaluated as part of the assessment visits at 0–1 months, 6 months and 12 months. We are aiming to complete study assessments to coincide with the infant's WIC certification and re-certification visits, required as part of their participation in the WIC Program, and as close to the targeted chronological age as possible (± 2 mo). In the event that it cannot be accomplished, we will extract the information from the participant's WIC record and document the source to avoid missingness. The use of this data source has already been contemplated in our informed consent as participants are asked to consent for us to extract information contained in their WIC record. The assessment visits are approximately 30 minutes and follow the study flowchart as shown in Figure 1.

Weight gain: The primary study outcome is adequate weight gain during the first year, as assessed using the weight-for-length z-score. Calibrated scales are used to measure weight (kg) and infantometers to measure length (cm) as made available by the WIC Program within their clinics. We are also measuring the infant's head and abdominal circumference at each study visit using a Gullick tape measure. For maternal anthropometrics, participants will self-report their weight prior to pregnancy and their weight at the beginning of pregnancy; however, weight at the 3rd trimester of pregnancy (when participants are recruited), will be measured by our research staff.

Objective assessment of infant activity and sleep patterns: We are objectively assessing the impact of the intervention on infant movement and sleep using accelerometers. We will provide the accelerometers and instructions during each of the assessment visits and we will collect them up at the participant's home or at another designated area suggested by the participant after they are done. We are using a novel approach that we have previously developed, and pilot tested in a group of 10 mother-infant dyads to objectively measure these components with excellent compliance [30,31]. The pilot study was used to develop the method of using the combination of two high-resolution triaxial accelerometers on the infant, one worn in the ankle and the other at the waist to distinguish infant movement from the infant being moved. The waist-worn monitor was able to reliably distinguish when the infant was lying versus being held during observed conditions as part of the pilot study (data not published). Infants will wear these devices for 3–5 days, starting at each assessment visit. We will use the high-resolution data from the accelerometer worn on the waist and ankle to determine the posture of the infant. This will be determined by calculating the angle of the accelerometers [32] and the magnitude of acceleration to distinguish when the infant is lying down vs. being held. We will use these data in effect to distinguish between infant movement and the infant being moved. At each measurement (0–1, 6 months, and 12 months) we will calculate an overall activity score, which is the percent of awake time moving assessed using the ankle-worn accelerometer; this will not include time that the infant is held. This measure assesses the infant's drive to move and it is the primary outcome for this component. We are also assessing the change from 0–1 months at each of these time points and quantify the intensity of movement by calculating the average vector magnitude during bouts of movement [33]. To quantify sleep patterns, we will calculate total sleep duration, the average length of a sleep bout and duration of individual sleep bouts [34].

Compliance will be assessed by the number of days that the accelerometer was worn by participants.

Physical activity and sleep questionnaire: We are also assessing the estimated time the infant spends in physical activities, sedentary behaviors and sleep using questionnaires; this is our secondary assessment of the infant activation. For this, we are using a questionnaire developed by our group and successfully implemented during the follow-up phase of a cohort study in 77 infants, 12 to 36 months of age in PR WIC [21]. This instrument includes questions related to the time and frequency the infant spends sleeping, in sedentary behaviors, and in physical activities. In addition, we have incorporated the Brief Infant Sleep Questionnaire (BISQ) to this assessment so that this aspect of the study is comparable to the Environmental Influences on Child Health Outcomes (ECHO)-wide cohorts. ECHO is funded by the National Institutes of Health (NIH). To determine the impact of improvements in infant sleep practices on maternal sleep practices, mothers enrolled in the intervention arm are being offered the opportunity to participate in an optional assessment. Those who agree are being asked to wear one accelerometer on a wrist for 14 days during the same time periods that their infant is wearing the assigned waist and ankle accelerometers. Also, for this sub-group of maternal participants, we are asking additional questions related to their sleep pattern and mental health history.

Infant Feeding Practices: this is assessed from the General Feeding Practices Questionnaire completed at each assessment visit. It contains questions about infant feeding (breast or bottle-feeding), type of milk used, age of stopping breastfeeding (exclusive and partial), age of introduction of juices and solid foods, use of the bottle to sleep baby, methods of feeding babies (i.e., using spoon, adding solids to bottle, etc.). This tool was developed by our group and tested among a sample of 296 infants [5].

Diet quality: it is assessed using a validated infant FFQ [35] at each assessment visit. This FFQ includes 52 food items with a brief description on how these were prepared and/or their source (e.g., raw, canned, etc.), portion sizes and supplements use. A Diet Quality Index Score was created based on this FFQ and validated among infants [20,36]. Maternal and infant medication exposure are also explored.

Self-efficacy questionnaire: a self-efficacy questionnaire was developed by our group for this study with questions about the healthy behaviors promoted as part of the intervention. This instrument was validated by experts and by face-validity (publication is being prepared). It is completed at the 12 months visit and includes questions on the self-efficacy for adopting the behaviors related to physical activity, sleep and response feeding.

Mental health: mood state and history of depression are assessed at the baseline visit and post-partum depression at the 6 months visit using the Spanish version of the Edinburg Depression Scale[37].

Access to basic services: We are also collecting information related to the participant's access to basic services that can impact the implementation of the study using the brief

screening tool of Accountable Health Communities Health-Related Social Needs and family support questions [38].

Exit interview: participants complete a short semi-structured qualitative interview at the end of the trial to provide the opportunity to make open comments about the web-platform and text messages sent. We ask about the videos, activities and messages that were most and least useful and how participants incorporated these into their infant care and rearing routines/practices. Additionally, we incorporated questions about family support, medical history and oral health.

Costs of the proposed intervention: To enable the translation of the intervention into a population-based standard of care, we are documenting the cost of development, maintenance and dissemination of the intervention. To obtain an accurate estimate of the cost of the intervention, we will determine the market value cost of the development of a distance-learning platform with the capabilities required to provide the intervention including development, hosting and service fees. We are also quantifying the time effort dedicated to each phase of the project and the personnel involved. The total cost of the platform will be calculated independently and only the service fee and the time effort of the individuals involved in on-going modifications (time effort of WIC officials will be used to determine opportunity cost, time effort of investigators will be considered consultant cost) will be incorporated into the calculation of the cost per participant. The remainder would be considered a one-time investment.

Our intervention plan incorporates a multimedia mobile technology platform, text messaging and regular phone calls. The interventionist records the amount of time dedicated to each task and this will be translated to a cost per participant in order to determine the overall cost of providing the intervention using the corresponding salary scale for a Puerto Rico WIC nutritionist. Alternate costs will be explored based on the potential of delegation of tasks to other members of the WIC staff. Our aim is to determine the total cost of the integration of the intervention to the program curriculum, taking into consideration current human resources available in all clinics.

Biorepository: a blood sample is being collected in infants at 0–1 months and at 12 months among those that agree to this optional collection for future analysis. A trained research nurse collects a capillary blood sample using dried blood spots. Future analysis may include metabolic (nutritional biomarkers including vitamins and lipid profiles), inflammatory, oxidative stress biomarkers as well as contribute to epigenetic assessments of lifestyle intervention trials of this currently understudied and genetically admixed population [39,40]. The selected method of bloodspot sample collection has been tested to achieve reliable samples for nutritional biomarker assessment, hormonal profiling, and methylation testing [41,42]. Also, samples of saliva, stool, nasal mucosa secretions and skin organisms will be collected at 0–1 months and at 12 months in infants and mothers that agree to this optional collection to enable future microbiome and metabolome studies. We also ask questions about the use of probiotics, antibiotics and medications during the study. Samples are stored at a –80°C freezer in a biorepository in the University of Puerto Rico Medical Sciences Campus.

Blinding

One of the main goals of the study is to demonstrate that this novel “infant activation” curriculum is translatable into routine care within the WIC program. To evaluate the effectiveness of the intervention with minimal risk of contamination, we have selected a cluster randomized design with randomization at the clinic level. Assessments are performed by blinded study staff in both control and intervention clinics. The interventionist notifies group allocation via a phone call to the participant to avoid unblinding of the assessment staff. Participants are oriented to avoid comments that would lead to disclosure of group allocation. The study investigators and biostatistics team are also be blinded to the intervention, with the exception of Dr. Palacios who oversees the Intervention. To ensure blinding, participant study identification numbers are provided in sequential fashion and only the unblinded personnel document the clinic assignment of each participant. The interventionist creates a dummy variable to categorize participants based on the type of clinic. All study and WIC clinic personnel are aware of the significance of maintaining assessors and blinding of study investigators.

Statistical analysis and data management

Power calculations.—A sample size of 20 participants per 10 clusters per arm (i.e., 400 participants among the control and intervention arms) achieved 80% power to detect a 15% difference in adequacy of weight gain between arms. This is taking into account a design with 3 repeated measurements and an unstructured covariance structure when the correlation between observations on the same subject is 0.01, and the alpha level is 0.05. This difference was estimated based on the study of Verbestel et al. [43] in which a 59% change percentage of the BMI z-score was found for their control arm. Different values of intra-cluster correlation coefficient (ICC) were used in order to estimate the detectable difference for BMI z-score between arms (Table 1); however, Murray et al. indicated that human studies usually have ICC values around 0.01 and 0.02 [44]. Stata v.14 was used to determine the detectable difference using the `clustersampsi` command.

To account for the different exclusion criteria, which are evaluated after the infant is born, such as premature birth (premature birth rate in Puerto Rico is 10–15%) and severe infant conditions, as well as participants lost to follow-up, we are over-recruiting pregnant women by 20%. Once 40% of the planned samples are collected, we will conduct interim analysis to verify and fine-tune the planned sample size, not to decide early termination of the study. The survey statistician (unblinded) will conduct the interim analysis and recommend a sample size adjustment, if necessary, to the study PIs. The final analysis will be conducted at an O’Brien-Fleming [45] alpha level 0.048.

Statistical Analysis of main outcomes.—Descriptive statistics will be used to characterize the study sample overall and for each arm. Mean, median and percentiles will be used for quantitative variables. Contingency tables will be used to describe the distribution of categorical data. Different graphs and plots will be used to better visualize data distribution. To assess the impact of the intervention on weight, infant activation, sleep and diet, a multilevel mixed-effects linear regression [46] will be performed to control the effect of the correlation among the WIC clinics (clusters) and the number of repeated

measures of the participants after 6 months and 12 months of the intervention, respectively. An assessment of interaction and confounding will be performed in these models. The mixed model will allow us to manage the presence of missing values (expected loss to follow up of 10–15%) [35,47], since it has no effect on other scores from the same participant. This approach, without any ad hoc imputation, has been considered more powerful than other intention-to-treat analysis options [48]. In addition, confidence intervals with 95% level will be used to present the average difference of the z-scores between intervention and non-intervention participants. All analyses will be performed using Stata software, version 13 (Stata Corporation, Washington, USA).

Data management and quality control: Study data is being collected and managed using REDCap (Research Electronic Data Capture) hosted by the Research Center for Minority Institution at the University of Puerto Rico, Medical Sciences Campus¹⁰⁵. De-identified data is entered in this system and investigators can access through a password-protected portal. A minimum number of trained users have access to enter data into the database.

Strategies for retention of participants

The research team has extensive experience in strategies for participant retention in long-term studies. For this study, we are using many of these same techniques, including: 1) keeping up to date lists of at least 3 contact persons for each participant; 2) sending text messages on important holidays; 3) study tokens with the study contact information; and 4) incentives. The principles that we are following in providing incentives are: 1) that they are large enough to fairly compensate for time spent but not be coercive and 2) that they are primarily for research assessment activities and not related to the intervention contacts, as we are evaluating if the intervention is sustainable without inordinate amounts incentives. Therefore, we are only providing incentives to participants related to their time-effort dedicated to study assessments with each participant receiving \$40 per completed visit starting from screening to study end and an additional \$15 for providing sample donations. Participants in the intervention arm do not receive additional incentives, as all intervention-related activities are being done leveraging technology and only in-person visits are being scheduled, if needed, for participants to trouble shoot issues with the web-platform.

Data and Participant Safety

The intervention and measurement protocols pose minimal risks to participants. Study design, recruitment strategies, and participant and data safety are monitored by the study investigators. They also ensure that the informed consent is obtained prior to performing any research procedures, that all subjects meet eligibility criteria, and that the study is conducted according to the IRB-approved research plan. The study investigators review the study conduct, such as accrual, drop-outs, protocol deviations, and compliance on a quarterly basis. All study personnel have been trained and certified in Mental Health First Aid as part of our Crisis Management Plan. Adverse events (AEs) are being reviewed individually in real-time and in aggregate on a quarterly basis. Although the study is very low risk, serious adverse events (SAEs) are also being reviewed in real-time. Protocol deviations, AEs, and SAEs are being reported to NIH and the IRB according to the applicable regulatory

requirements. However, there are no expected AEs associated with the intervention. Safety alerts include disclosure of personal information, bleeding, minor bruising, pain, inflammation or soreness in the area associated with blood drawn, post-partum depression, and minimal discomfort and skin irritation when wearing the accelerometers.

DISCUSSION

The Baby-Act trial will determine the effects of an intervention that combines key messages and activities designed to promote sound parenting skills that support and sustain healthy lifestyle beyond what is offered by WIC such as ‘infant activation’, sleep and response feeding in the first year of life for promoting healthy weight gain. This is particularly important as the first 1,000 days of life provide a unique window of opportunity to establish life-long healthy lifestyle patterns. Given the metabolic programming that occurs at this stage of life, together with the behavioral modeling pliability during infancy, intervening at this age may be the most critical and potentially efficacious window of opportunity for true obesity prevention [12].

Few dietary interventions for preventing excessive weight in infants have been effective. Interventions to prevent obesity are most effective when they start early in life; yet, there are only few effective interventions specifically geared to prevent obesity during the first 1,000 days of life [12,13]. Among several published interventions during the first 1,000 days of life to prevent overweight/obesity, only a few were effective [49]. Effective interventions focused mainly on behavioral change at the individual/family level through home visits, a combination of individual and group counseling sessions at the clinical setting, or combination of home and group sessions. However, most trials were face-to-face, underpowered, with low compliance and adherence to the interventions, and only increasing knowledge without increasing skills. Most did not include Hispanics, a high-risk group for early development of obesity. Furthermore, only a few targeted early-life systems and policies, which make the translation of such interventions into currently available programs difficult.

In addition, there is a very limited number of interventions focusing on increasing physical activity in infants [14–16]. The InFANT (Melbourne Infant Feeding, Activity, and Nutrition Trial) among 542 parents and their infants included six 2-hour sessions to build parenting knowledge, skills and social support for 20 months [15,16]. No difference in BMI z-score was found between intervention and control groups, although small improvements were seen. An even greater gap exists in relation to the capacity to objectively measure changes in infant physical activity, sleep patterns and sedentary behavior through the use of accelerometry. The SLIMTIME (SLeeping and Intake Methods Taught to Infants and Mothers Early in Life) Intervention is one of the few studies including accelerometry [14]. This trial was conducted in the US through home nurse visits among 160 mother-infant’s dyads. Participants were randomized to receive: 1) soothing strategies in response to fussiness, 2) instructions for delaying complementary foods until 4 months and avoiding putting infant cereal into bottles, 3) both interventions, or 4) none for 12 months. Those receiving both interventions had lower weight-for-length compared to the other three groups, suggesting that multicomponent interventions are more effective.

WIC is fundamental in reaching out to low-income pregnant, infants and children up to age 5. As mentioned previously, participation in the WIC program in Puerto Rico is very high (79%), reaching all low-income young children [18]. In addition, WIC clinics are likely to be ideal sites for implementing effective interventions among infants. In fact, there are some effective interventions done through WIC to improve fruit and vegetable intake [50] and physical activity [51] among postpartum women, to improve breastfeeding [52] and to improve certain feeding practices, such as feeding the baby with the spoon (35% in interventions vs. 20% in controls; $p < 0.05$) [53]. Also, a recent report from the CDC showed that adjusted obesity prevalence in Puerto Rico decreased among children aged 2–4 years by 8.2 percentage points from 2010 to 2016; the greatest reduction of all states and territories [3]. Therefore, the Baby-Act trial has the potential to help reduce this even further by intervening earlier in life.

In conclusion, the Baby-Act trial will be the first study to test the addition of complementary approaches associated with early childhood obesity to the current WIC standard of care. This is particularly important in Hispanics, an under-represented high-risk group with generally high prevalence of obesity. Our intervention, which begins with participants during pregnancy, will improve parenting skills before delivery, influencing behaviors such as infant activity, sedentary time, sleep patterns, and infant feeding practices. Early dissemination is also expected to improve the modeling of healthy behaviors from parent to child and break the intergenerational patterns of obesity observed among at-risk women and their offspring [54]. This intervention also has the potential to inform and influence other WIC programs with similar populations at the national level to enhance WIC services to all program participants. If successful, the proposed intervention could be adopted as part of the certification and re-certification visits, with the distance learning component integrated into the WIC website, among these groups.

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References

- [1]. World Health Organization (WHO). Childhood obesity panel: 40 million kids under 5 overweight, (n.d.). <http://www.businessinsider.com/ap-childhood-obesity-panel-40-million-kids-under-5-overweight-2016-1> (accessed January 29, 2016).
- [2]. Johnson B, thorn B, McGill B, Suchman A, Mendelson M, Patlan KL, Freeman B, Gotlieb R, Connor P, WIC Participant and Program Characteristics 2012, U.S. Department of Agriculture, Food and Nutrition Service, Alexandria, VA, 2013.
- [3]. Pan L, Blanck HM, Park S, Galuska DA, Freedman DS, Potter A, Petersen R, State-Specific Prevalence of Obesity Among Children Aged 2–4 Years Enrolled in the Special Supplemental

- Nutrition Program for Women, Infants, and Children - United States, 2010–2016, MMWR. Morb. Mortal. Wkly. Rep. 68 (2019) 1057–1061. 10.15585/mmwr.mm6846a3. [PubMed: 31751324]
- [4]. Ogden CL, Carroll MD, Kit BK, Flegal KM, Prevalence of childhood and adult obesity in the United States, 2011–2012, J. Am. Med. Assoc. 311 (2014) 806–814. 10.1001/jama.2014.732 [doi].
- [5]. Sinigaglia OE, Ríos EM, Campos M, Díaz B, Palacios C, Breastfeeding practices, timing of introduction of complementary beverages and foods and weight status in infants and toddlers participants of a WIC clinic in Puerto Rico, Springerplus. 5 (2016) 1437 10.1186/s40064-016-3154-9. [PubMed: 27652013]
- [6]. Nader PR, O'Brien M, Houts R, Bradley R, Belsky J, Crosnoe R, Friedman S, Mei Z, Susman E.J., of C.N.I.H. and H.D.E.C.C.R. Network, Identifying risk for obesity in early childhood, Pediatrics. 118 (2006) e594–601. <https://doi.org/10.1542/peds.2005-2801> [pii]; 10.1542/peds.2005-2801 [doi]. [PubMed: 16950951]
- [7]. Stettler N, Zemel BS, Kumanyika S, Stallings VA, Infant weight gain and childhood overweight status in a multicenter, cohort study, Pediatrics. 109 (2002) 194–199. [PubMed: 11826195]
- [8]. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH, Predicting obesity in young adulthood from childhood and parental obesity, N. Engl. J. Med. 337 (1997) 869–873. 10.1056/NEJM199709253371301 [doi]. [PubMed: 9302300]
- [9]. Ong KK, Loos RJF, Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions., Acta Paediatr. 95 (2006) 904–8. 10.1080/08035250600719754. [PubMed: 16882560]
- [10]. Snethen JA, Hewitt JB, Goretzke M, Childhood obesity: the infancy connection, J. Obstet. Gynecol. Neonatal Nurs. 36 (2007) 501–510. <https://doi.org/10.1016/j.jog.2007.05.001> [pii].
- [11]. Taveras EM, Gillman MW, Kleinman K, Rich-Edwards JW, Rifas-Shiman SL, Racial/ethnic differences in early-life risk factors for childhood obesity, Pediatrics. 125 (2010) 686–695. 10.1542/peds.2009-2100 [doi]. [PubMed: 20194284]
- [12]. Dattilo AM, Birch L, Krebs NF, Lake A, Taveras EM, Saavedra JM, Need for Early Interventions in the Prevention of Pediatric Overweight : A Review and Upcoming Directions, J. Obes. 2012 (2012) 1–18. 10.1155/2012/123023.
- [13]. Ciampa PJ, Kumar D, Barkin SL, Sanders LM, Yin HS, Perrin EM, Rothman RL, Interventions aimed at decreasing obesity in children younger than 2 years: a systematic review., Arch. Pediatr. Adolesc. Med. 164 (2010) 1098–104. 10.1001/archpediatrics.2010.232. [PubMed: 21135337]
- [14]. Paul IM, Savage JS, Anzman SL, Beiler JS, Marini ME, Stokes JL, Birch LL, Preventing obesity during infancy: a pilot study., Obesity (Silver Spring). 19 (2011) 353–61. 10.1038/oby.2010.182. [PubMed: 20725058]
- [15]. Campbell K, Hesketh K, Crawford D, Salmon J, Ball K, McCallum Z, The Infant Feeding Activity and Nutrition Trial (INFANT) an early intervention to prevent childhood obesity: cluster-randomised controlled trial., BMC Public Health. 8 (2008) 103 10.1186/1471-2458-8-103. [PubMed: 18373877]
- [16]. Campbell KJ, Lioret S, McNaughton SA, Crawford DA, Salmon J, Ball K, McCallum Z, Gerner BE, Spence AC, Cameron AJ, Hnatiuk JA, Ukoumunne OC, Gold L, Abbott G, Hesketh KD, A parent-focused intervention to reduce infant obesity risk behaviors: a randomized trial, Pediatrics. 131 (2013) 652–660. 10.1542/peds.2012-2576 [doi]. [PubMed: 23460688]
- [17]. EM T, P. M, JA WB, The Impact of the First 1,000 Days on Childhood Obesity, Durham, NC, 2016 www.healthyeatingresearch.org (accessed January 12, 2017).
- [18]. Betson D, Martinez-Schiferl M, and Giannarelli L, Zedlewski S, National- and State-Level Estimates of Eligibility and Program Reach, 2000–2009, Washington, DC, 2011 <http://www.urban.org/research/publication/national-and-state-level-estimates-wic-eligibles-and-program-reach-2000-2009> (accessed September 18, 2015).
- [19]. USDA, WIC BREASTFEEDING DATA LOCAL AGENCY REPORT, (2016). <http://www.fns.usda.gov/sites/default/files/wic/FY2015BFDLAREport.pdf> (accessed December 16, 2016).
- [20]. Rios E, Sinigaglia O, Diaz B, Campos M, Palacios C, Development of a Diet Quality Score for Infants and Toddlers and its Association with Weight, J. Nutr. Heal. Food Sci. 4 (2016) 1–7. .

- [21]. Molina J, Amaro K, Pérez CM, Palacios C, Sleep Duration, Sedentary Behaviors, and Physical Activity across Weight Status in Hispanic Toddlers' Participants of the WIC Program, *J. Child. Obes.* 1 (2016). <http://childhood-obesity.imedpub.com/sleep-duration-sedentary-behaviors-and-physical-activity-across-weight-status-in-hispanic-toddlers-participants-of-the-wic-program.pdf> (accessed December 16, 2016).
- [22]. Andersen PK, 1. Design and Analysis of Cluster Randomization Trials in Health Research. Allan Donner and Neil Klar, Arnold, London, 2000. No. of pages: x+178. Price:£35.ISBN 0–340-691530, *Stat. Med.* 21 (2002) 1961–1962. 10.1002/sim.957.
- [23]. U.S. Census Bureau, QuickFacts: Puerto Rico, 2020 (n.d.). <https://www.census.gov/quickfacts/PR> (accessed September 8, 2020).
- [24]. Tucker CM, Rice KG, Hou W, Kaye LB, Nolan SEM, Grandoit DJ, Gonzales L, Smith MB, Desmond FF, Development of the Motivators of and Barriers to Health-Smart Behaviors Inventory., *Psychol. Assess.* 23 (2011) 487–503. 10.1037/a0022299. [PubMed: 21443361]
- [25]. Bandura A, Self-efficacy: toward a unifying theory of behavioral change., *Psychol. Rev.* 84 (1977) 191–215. <http://www.ncbi.nlm.nih.gov/pubmed/847061> (accessed December 7, 2016). [PubMed: 847061]
- [26]. Fogg B, Creating Persuasive Technologies: An Eight-Step Design Process, (n.d.). www.bjfogg.com (accessed December 7, 2016).
- [27]. Oinas-Kukkonen H, Harjumaa M, LNCS 5033 - A Systematic Framework for Designing and Evaluating Persuasive Systems, LNCS. 5033 (2008) 164–176.
- [28]. Florez-Arango JF, Iyengar MS, Dunn K, Zhang J, Performance factors of mobile rich media job aids for community health workers, *J. Am. Med. Informatics Assoc.* 18 (2011) 131–137. 10.1136/jamia.2010.010025.
- [29]. Iyengar M, Florez-Arango J, Persuasive Aspects of a rich-media mobile health system., in: *Persuasive2010*, Copenhagen, Denmark, 6 2010, 2010.
- [30]. Torres R, Soltero S, Trak MA, Tucker CM, Mendez K, Campos M, Willett W, Melendez M, Gillman MW, Franks PW, Joshupura K, Pomeroy J, Palacios C, Lifestyle modification intervention for overweight and obese Hispanic pregnant women: development, implementation, lessons learned and future applications., *Contemp. Clin. Trials Commun.* 3 (2016) 111–116. 10.1016/j.conctc.2016.05.004. [PubMed: 27822567]
- [31]. Trak-Fellermeier MA, Campos M, Meléndez M, Pomeroy J, Palacios C, Rivera-Viñas J, Méndez K, Febo I, Willett W, Gillman MW, Franks PW, Joshupura K, PEARLS randomized lifestyle trial in pregnant Hispanic women with overweight/obesity: gestational weight gain and offspring birthweight, *Diabetes, Metab. Syndr. Obes. Targets Ther.* Volume 12 (2019) 225–238. 10.2147/DMSO.S179009.
- [32]. Fisher CJ, Using an Accelerometer for Inclination Sensing, AN-1057, Appl. Note, Analog Devices. (2010).
- [33]. van Hees VT, Gorzelniak L, Dean León EC, Eder M, Pias M, Taherian S, Ekelund U, Renström F, Franks PW, Horsch A, Brage S, Separating Movement and Gravity Components in an Acceleration Signal and Implications for the Assessment of Human Daily Physical Activity, *PLoS One.* 8 (2013) e61691 10.1371/journal.pone.0061691. [PubMed: 23626718]
- [34]. Galland BC, Kennedy GJ, Mitchell EA, Taylor BJ, Algorithms for using an activity-based accelerometer for identification of infant sleep-wake states during nap studies, *Sleep Med.* 13 (2012) 743–751. 10.1016/j.sleep.2012.01.018. [PubMed: 22542788]
- [35]. Palacios C, Sinigaglia O, Ríos E, Santiago-Rodríguez E, Rivas-Tumanyan S, Campos M, Diaz B, Willett WC, Validity of a semi-quantitative food frequency questionnaire (FFQ) for Hispanic infants 0–24 months, *J. Acad. Nutr. Diet.* In Review (2016).
- [36]. Amaro K, Molina J, Perez C, Palacios C, Longitudinal associations between dietary patterns and weight status in Hispanic infants and toddlers' participants of the WIC Program, *Matern. Child Health J.* (n.d.).
- [37]. Vega-Dienstmaier JM, Mazzotti Suárez G, Campos Sánchez M, Validación de una versión en español de la escala de depresión postnatal de edimburgo, *Actas Esp. Psiquiatr.* 30 (2002) 106–111. <https://pubmed.ncbi.nlm.nih.gov/12028943/> (accessed September 8, 2020). [PubMed: 12028943]

- [38]. Billioux A, Verlander K, Anthony S, Alley D, Standardized Screening for Health-Related Social Needs in Clinical Settings The Accountable Health Communities Screening Tool, 2017.
- [39]. Moreno-Estrada A, Gravel S, Zakharia F, McCauley JL, Byrnes JK, Gignoux CR, Ortiz-Tello PA, Martínez RJ, Hedges DJ, Morris RW, Eng C, Sandoval K, Acevedo-Acevedo S, Norman PJ, Layrisse Z, Parham P, Martínez-Cruzado JC, Burchard EG, Cuccaro ML, Martin ER, Bustamante CD, Reconstructing the Population Genetic History of the Caribbean, *PLOS Genet.* 9 (2013) 1–19. 10.1371/journal.pgen.1003925.
- [40]. Via M, Gignoux CR, Roth LA, Fejerman L, Galanter J, Choudhry S, Toro-Labrador G, Viera-Vera J, Oleksyk TK, Beckman K, Ziv E, Risch N, Burchard EG, Martínez-Cruzado JC, History Shaped the Geographic Distribution of Genomic Admixture on the Island of Puerto Rico, *PLoS One.* 6 (2011) 1–8. 10.1371/journal.pone.0016513.
- [41]. Holen T, Norheim F, Gundersen TE, Mitry P, Linseisen J, Iversen PO, Drevon CA, Biomarkers for nutrient intake with focus on alternative sampling techniques, *Genes & Nutr.* 11 (2016) 12 10.1186/s12263-016-0527-1.
- [42]. Staunstrup NH, Starnawska A, Nyegaard M, Christiansen L, Nielsen AL, Børghlum A, Mors O, Genome-wide DNA methylation profiling with MeDIP-seq using archived dried blood spots, *Clin. Epigenetics.* 8 (2016) 81 10.1186/s13148-016-0242-1. [PubMed: 27462375]
- [43]. Verbestel V, De Coen V, Van Winckel M, Huybrechts I, Maes L, De Bourdeaudhuij I, Prevention of overweight in children younger than 2 years old: a pilot cluster-randomized controlled trial, *Public Health Nutr.* 17 (2014) 1384–1392. 10.1017/S1368980013001353. [PubMed: 23701835]
- [44]. Murray DM, Rooney BL, Hannan PJ, V Peterson A, V Ary D, Biglan A, Botvin GJ, Evans RI, Flay BR, Futterman R, Intraclass correlation among common measures of adolescent smoking: estimates, correlates, and applications in smoking prevention studies., *Am. J. Epidemiol.* 140 (1994) 1038–50. <http://www.ncbi.nlm.nih.gov/pubmed/7985652> (accessed February 1, 2017). [PubMed: 7985652]
- [45]. O'Brien PC, Fleming TR, A multiple testing procedure for clinical trials., *Biometrics.* 35 (1979) 549–56. <http://www.ncbi.nlm.nih.gov/pubmed/497341> (accessed February 2, 2017). [PubMed: 497341]
- [46]. Snijders TAB, R.J. (Bosker Roel J., Multilevel analysis : an introduction to basic and advanced multilevel modeling, Sage, 2012.
- [47]. Banna J, Campos M, Gibby C, Graulau RE, Meléndez M, Reyes A, Lee JE, Palacios C, Multi-site trial using short mobile messages (SMS) to improve infant weight in low-income minorities: Development, implementation, lessons learned and future applications., *Contemp. Clin. Trials.* 62 (2017) 56–60. 10.1016/j.cct.2017.08.011. [PubMed: 28827160]
- [48]. Chakraborty H, Gu H, A Mixed Model Approach for Intent-to-Treat Analysis in Longitudinal Clinical Trials with Missing Values, RTI Press publication MR-0009–0903, Research Triangle Institute, Research Triangle Park, NC, USA, 2009.
- [49]. Blake-Lamb TL, Locks LM, Perkins ME, Woo Baidal JA, Cheng ER, Taveras EM, Interventions for Childhood Obesity in the First 1,000 Days A Systematic Review., *Am. J. Prev. Med.* 50 (2016) 780–9. 10.1016/j.amepre.2015.11.010. [PubMed: 26916260]
- [50]. Herman DR, Harrison GG, Afifi AA, Jenks E, Effect of a targeted subsidy on intake of fruits and vegetables among low-income women in the Special Supplemental Nutrition Program for Women, Infants, and Children., *Am. J. Public Health.* 98 (2008) 98–105. 10.2105/AJPH.2005.079418. [PubMed: 18048803]
- [51]. Albright CL, Maddock JE, Nigg CR, Increasing physical activity in postpartum multiethnic women in Hawaii: results from a pilot study., *BMC Womens. Health.* 9 (2009) 4 10.1186/1472-6874-9-4. [PubMed: 19254387]
- [52]. Reeder JA, Joyce T, Sibley K, Arnold D, Altindag O, Telephone peer counseling of breastfeeding among WIC participants: a randomized controlled trial., *Pediatrics.* 134 (2014) e700–9. 10.1542/peds.2013-4146. [PubMed: 25092936]
- [53]. Palacios C, Campos M, Gibby C, Meléndez M, Lee JE, Banna J, Effect of a Multi-Site Trial using Short Message Service (SMS) on Infant Feeding Practices and Weight Gain in Low-Income Minorities, *J. Am. Coll. Nutr.* 30 (2018) 1–9. 10.1080/07315724.2018.1454353.

- [54]. Fox M, Entringer S, Buss C, DeHaene J, Wadhwa PD, Intergenerational transmission of the effects of acculturation on health in Hispanic Americans: a fetal programming perspective., *Am. J. Public Health.* (2015) S409–23. 10.2105/AJPH.2015.302571. [PubMed: 25905831]

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Figure 1.
Study flow

Table 1.

Detectable difference in BMI z-score change percentage based on a baseline difference of 59%, an alpha of 0.05, 80% statistical power, 10 clusters per arm, and 20 participants per cluster.

Intra class correlation	Detectable difference (increased) in change %
0.01	15
0.02	16
0.03	17
0.04	18