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Prepare, a randomized trial to promote and evaluate weight loss among overweight and obese women planning pregnancy: Study design and rationale

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Abstract

Background—Women who are overweight or have obesity at pregnancy onset, and those who gain excessive weight during pregnancy, are at increased risk of pregnancy-related complications and large for gestational age infants.

Objective—This report describes methodology for the Prepare study, a randomized, controlled clinical trial testing a preconception and pregnancy weight management program for women who are overweight or have obesity (BMI ≥ 27 kg/m^2).

Outcomes—This trial examines multiple pregnancy and neonatal outcomes, with the primary outcome being gestational weight gain (GWG). Secondary outcomes include change in weight before conception, offspring birth weight adjusted for gestational age, offspring weight for length, and pregnancy diet quality and physical activity level.

Methods—Nonpregnant women who anticipate becoming pregnant in the next 2 years are randomly assigned to an intervention program or a usual care control condition. Intervention participants receive weight management counseling by telephone before and during pregnancy, with weekly contacts during the first 6 months and monthly contacts for the next 18 months. Intervention participants also have unlimited access to a study website that provides self-management tools. All participants who become pregnant are contacted at 20 weeks' gestation to assess physical activity levels and dietary habits. All other outcome data are obtained from medical records. Intervention satisfaction is assessed via questionnaire.

Summary—This clinical trial tests the efficacy of an intervention program designed to help overweight and obese women achieve healthy lifestyle changes that will result in a healthy weight prior to pregnancy and appropriate weight gain during pregnancy.

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Keywords

Weight loss; Prenatal; Pregnancy

1. Introduction

More than 55% of reproductive-aged women in the U.S. are overweight or have obesity [1]. Growing evidence suggests that being overweight or having obesity at pregnancy onset, and excessive weight gain during pregnancy, increases the risk of pregnancy-related complications such as gestational diabetes and pre-eclampsia [2-4], and a substantially increased risk of future obesity and its consequences in offspring [5-7] and mothers [8].

Systematic reviews have focused on the effects of intervening on diet and other lifestyle habits during pregnancy in order to curb excessive gestational weight gain (GWG); results have been mixed [9-13]. While the most recent meta-analysis found that lifestyle counseling during pregnancy can reduce risk of excessive GWG [13], the decrease in GWG with pregnancy lifestyle interventions often is not at current Institute of Medicine guidelines [14]. In our own Healthy Moms trial, women randomized to a healthy lifestyle intervention starting at around 15 weeks' gestation were more likely to be within IOM weight gain guidelines compared to usual care, but 44% of women still gained above the recommended amount [15]. Also, the effect of pregnancy lifestyle counseling on large for gestational age (LGA) and macrosomia in infants is unclear. LGA and macrosomia place infants at risk for neonatal hypoglycemia requiring medical intervention [16], and in the long term, infants may be at increased risk for childhood obesity and metabolic syndrome [17]. LGA is also associated with an increased risk of cesarean delivery, postpartum hemorrhage, and shoulder dystocia, which can result in newborn clavicular fracture and brachial plexus injury [16] While one recent review and our own Healthy Moms trial found a reduction in risk of macrosomia or LGA in high-risk women given a lifestyle intervention [10, 15], another meta-analysis did not find differences in infant birth weight [13].

Part of the reason that the success of pregnancy lifestyle programs, including our Healthy Moms trial, is limited may be that a mother's pre-pregnancy and early pregnancy metabolic conditions are as important or more important than GWG in influencing fetal overgrowth [18]. Pre-pregnancy Body Mass Index (BMI) influences early placenta function, inflammation, and gene expression in the first trimester [14], prior to the first prenatal visit, when most pregnancy intervention trials are initiated. We developed this pre-pregnancy study because we hypothesized that initiating a weight loss intervention *prior to* pregnancy would be more effective than starting the intervention *during* pregnancy. Starting pregnancy with a normal BMI, healthy diet, and appropriate physical activity level may increase the likelihood of achieving GWG within IOM guidelines [19, 20] and fewer pregnancy and neonatal complications. Indeed, women who have lost weight between pregnancies, especially those who have lost significant amounts of weight after anti-obesity surgery, experience fewer complications compared to women who did not lose weight between pregnancies [21-24].

The IOM and other agencies recommend that women should reach a healthy weight before conceiving. Yet there is a paucity of prospective trials demonstrating the value of preconception weight loss in improving pregnancy outcomes. A 2014 systematic evidence review identified only a single preconception intervention trial; however, even this trial was not focused on weight loss per se but on improving poor nutrition, low physical activity, tobacco and alcohol use and exposure, unhealthy coping with stress, gynecologic infections, and inadequate pregnancy planning or spacing [13, 25]. Several recent trials have examined the effects of weight loss intervention on fertility rates in infertile women, but have not presented data on GWG or pregnancy outcomes [26-29]. To fill this research gap, we are conducting a randomized clinical trial, Prepare, to evaluate a comprehensive preconception weight-loss program. The intervention program being tested has been designed to help women who are overweight or have obesity (BMI ≥ 27 kg/m^2) adopt improved dietary and physical activity habits and lose weight in preparation for pregnancy, and then to maintain these new behaviors during pregnancy to avoid excessive GWG. Women of reproductive age have many demands on their time (family, work, etc.) and their attendance may be low when counseling is provided in a group format [30-32]. Thus, the active intervention in Prepare employs a combination of telephone counseling by trained health coaches and a supportive website in lieu of group counseling [33-35].

This report describes the development and methodology for the Prepare study (clinical govs number NCT02346162). The Kaiser Permanente Northwest Institutional Review Board approved the study and all consent procedures. All study procedures are carried out in accord with the Code of.

Ethics of the World Medical Association (Declaration of Helsinki) [36]. A Data Safety Monitoring Board (DSMB) is overseeing the study, and can suggest early termination if there are serious adverse effects in the entire intervention group or in a dominating subgroup, futility of study because of recruitment issues, or logistical or data quality problems so severe that correction is not feasible.

2. Study design

2.1 Study aims

Our primary aim is to implement a randomized clinical trial (RCT) to test the efficacy of a weight management intervention in comparison to usual care control for overweight and obese (BMI ≥ 27 kg/m^2) women planning a pregnancy in the next two years. We hypothesize that women in the preconception weight-loss intervention group will be more likely to be within target IOM GWG recommendations than women randomized to usual care control. As a secondary hypothesis, we believe women in the intervention group will have lower weights at their first prenatal visit (proxy for conception weight) than usual care participants and will have offspring with lower birth weights (closer to national norms) than offspring of usual care control mothers. Our secondary aim is to compare diet and exercise patterns of intervention and usual care control participants in the second trimester of pregnancy. We hypothesize that a preconception weight-loss intervention delivered through telephone and electronic media will favorably influence women's dietary intake and physical activity levels, as evidenced by intervention participants being closer to their goal caloric

intake, eating more servings of fruit and vegetables and less saturated fat, and engaging in more moderate intensity exercise compared to usual care controls. Our final aim is to evaluate the acceptability of the intervention for implementation in routine health care. We hypothesize that because it is adaptable to busy lifestyles, a preconception weight-loss intervention delivered mainly through telephone and electronic media will have high overall program satisfaction and women will be highly willing to refer others considering pregnancy to such a program.

2.2 Study population

We are recruiting participants from the Kaiser Permanente Northwest (KPNW) population.

KPNW is a not-for-profit, group-model health maintenance organization that provides integrated, comprehensive medical care to > 500,000 individuals within a 75-mile radius of Portland, Oregon. To be eligible for Prepare, women must be KPNW members, between the ages of 18–40, and considering pregnancy within the next 2 years, and meet other eligibility criteria shown in Table 1.

2.3 Recruitment and randomization

Based on data from the Healthy Moms trial [15], we estimate we need a sample size of 75 pregnancies per arm in order to detect a 20.5% difference in the number of women who do not exceed GWG guidelines in the intervention and usual care control groups (power of 0.8 at alpha level of .05). In the Healthy Moms study, 17% participants in the usual care arm did not exceed GWG guidelines compared to 56% in the intervention arm (39% difference) [37]. With a sample size of 75 per group, we'll be able to achieve 80% power to detect a significant mean difference of 0.46 in weight for gestational age z-score between the two groups when assuming a standard deviation of 1.0 and alpha level of 0.05.

Potential participants for the prepare trial are identified via KPNW medical record data. Recruitment includes women in the target age range whose most recent (within 4 years) BMI was 27 kg/m^2 or greater and who have treatment codes indicating that they might be considering pregnancy (i.e., preconception counseling visit, IUD removal, prenatal genetic screening, pregnancy in the last two years). If necessary to attain recruitment goals, we will also reach out to women in the target age and BMI range even if they do not have the treatment codes. Potential participants are sent a recruitment letter, followed 3 days later by a recruitment email. Three additional email recruitment efforts are made at 6-week intervals, supplemented with telephone text messages 10 weeks and 20 weeks after the initial recruitment letter. In addition to these recruitment messages, we encourage KPNW primary care and OB/GYN physicians to inform their patients about the study.

Recruitment materials prompt women to go to the prepare study websitewww.preparestudy.org), which describes the trial and allows women to self-screen for study eligibility. Those who meet eligibility requirements are invited to sign up for a group information session. These sessions, offered once a week, are led by a project investigator who describes the study in detail and answers participant questions. Attendance is required to join the study. Interested women are then scheduled to return for a screening, baseline, and randomization visit in approximately 1 week.

Prior to the screening/baseline/randomization visit, potential participants must complete a set of baseline questionnaires about their health history and current physical activity [38], and complete two 24-hour online food recalls (http://epi.grants.cancer.gov/asa24/).

2.3.1 Baseline visit and randomization—At the screening/baseline/randomization visit, project staff determine eligibility (Table 1), obtain signed informed consent, ensure that all study questionnaires and food recalls are complete, and measure participants' height and weight to confirm BMI ≥ 27 kg/m^2. Group assignments are made in a 1:1 ratio via a random, computerized sequence generation process designed by the study statistician. Randomization is stratified by age (<30, 30+), BMI (27-30, 31-35, 36+ kg/m^2), and parity (0, 1+) and allocation is concealed until the randomization button is pressed. Women assigned to the control condition receive brief verbal and written information on how to have a healthy pregnancy (e.g., adequate folic acid intake, issues regarding adequate and safe fish intake, general nutrition guidance, adequate fluid intake, safe and adequate physical activity, smoking cessation, and health maintenance)[39] but are not contacted further unless they become pregnant (data collection midway through pregnancy). Participants assigned to the intervention group receive the same information as the control participants. They also begin active intervention with an in-person counseling session.

2.4 Intervention goals, approach, and rationale

2.4.1 Intervention goals—In this two-year, comprehensive, frequent-contact intervention, participants receive health coach counseling to promote the overall intervention goals (Table 2), which were designed to promote prenatal weight loss and GWG according to IOM guidelines during pregnancy.

2.4.2 Weight management intervention

2.4.2.1 Health coach in-person session(s): The intervention starts immediately after randomization with an in-person counseling session, at which the health coach explains the overall intervention goals (Table 2) and calculates the participant's weight loss and calorie goals. The health coach reviews resources for self-tracking diet and exercise, with women being encouraged to track in the way that is most convenient for them. We do not record what tracking method they use.

The health coach also familiarizes the participant with the study's intervention website. The session ends with the coach scheduling a phone conversation and helping the participant establish an initial diet and exercise plan for the week. After the initial session, the intervention is conducted by telephone.

2.4.2.2 Health coach phone appointments supported by a website: Phone appointments, which are pre-scheduled at times convenient to participants, occur weekly for the first 6 months and then monthly for the next 18 months. Participants have unlimited access to a password-protected interactive and informative study website. Health coaches encourage them to log into the website between weekly phone appointments to enter weight, number of days they kept food records, and exercise minutes and steps. The website uses information that participants enter to display feedback graphs of individual progress. Health coaches

have access to participant graphs and review weekly progress with participants during the phone appointments. Additionally, weekly goals and plans are established and displayed on participants' website accounts. Information modules in the form of downloadable worksheets are also accessible on the website. These modules cover nutrition, exercise, behavior change, and pregnancy topics. The modules are adapted from our successful Healthy Moms curriculum [15], which was, in turn, based on the weight loss program in the WLM Trial [40-42].

Counseling phone calls apply principles of social cognitive theory [43] and the techniques of behavioral self-management [44]. These approaches assist participants in setting reasonable short-term goals, formulating specific action plans, self-monitoring progress, and evaluating and modifying plans to promote progress over time [43-45]. Health coaches develop participant motivation and commitment to change using motivational interviewing techniques [46-48]. The FRAMES model (Feedback, Responsibility, Advice, Menu of options, Empathy, and Self-Efficacy) provides a conceptual structure for how coaches tailor intervention goals to accommodate varying degrees of readiness to change [46-48].

Each 20 to 30 minute call follows counseling model consisting of five steps. The health coach first assesses the woman's current diet and physical activity, and motivation for change [45, 48]. The coach works collaboratively with the participant to set specific goals to ensure participant engagement [43-48] and guides the participant in identifying social-environmental supports and personal/family barriers to accomplish mutually agreed-upon dietary and physical activity goals in step 3 [48]. The participant then develops personalized problem-solving strategies [43-49]. In the final step, the coach provides follow-up support, accountability, and feedback [43-49].

2.4.2.3 Overall intervention goals (Table 2): The overall goals are two-fold: prenatal weight loss and gestational weight management. For prenatal weight loss, intervention participants have frequent contact with a health coach, working toward the long-term goal of losing 10% or more of their randomization weight, or achieving a BMI of 25 kg/m^2, whichever comes first. Participants work with their health coach to customize a dietary plan at an appropriate caloric level for healthy and safe weight loss (0.5 – 2.0 lb per week). The intervention includes a recommendation that participants engage in a moderately intensive physical activity, working toward a goal of 60 min per day, that they can continue safely into pregnancy. We also encourage participants to use a pedometer to work toward a daily goal of at least 10,000 steps (which is about 5 miles or 100 min of walking at a speed of 20-minute mile). If women are breast-feeding, their calorie goal is adjusted to account for the additional calories needed for milk production and calorie goals are kept above 1500 kcal [50, 51]. When an intervention participant becomes pregnant, the goal is switched to gestational weight management and the health coach uses the calls to alter the dietary plan and calorie level as needed to achieve GWG within current IOM guidelines [52].

2.4.2.4 Nutrition goals: Dietary Approaches to Stop Hypertension (DASH) dietary pattern: Consumption of whole foods such as fruits, vegetables, low-fat dairy and lean meats before and throughout pregnancy has been shown to be beneficial for appropriate infant birth weight.[53] Therefore, based on guidelines provided by the American College of

Obstetrics & Gynecology (ACOG) [54], and the US Department of Agriculture (USDA) Dietary Guidelines for Americans 2010 [55], we chose to encourage our participants to follow the DASH dietary pattern (without sodium restriction). The DASH dietary plan is nutrient dense, has sufficient amounts of carbohydrates, healthier levels and types of fat, and limits added sugars, and is flexible, allowing adjustment, if needed, to enhance glucose control and prevent ketonemia during pregnancy. This dietary pattern was used successfully during pregnancy in the Healthy Moms study [15]. As an added benefit, by incorporating the DASH dietary pattern into their lives, women (and presumably their families) will enjoy important long-term health benefits because adherence to the DASH dietary pattern has been associated with a lower risk of CHD and stroke over long-term follow-up [56].

2.4.2.5 Diet and weight loss goals before pregnancy: Initial calorie needs are set using the Harris-Benedict equation [57]. Coaches modify calorie targets as needed to meet weight loss and maintenance goals, as well as GWG goals. They also provide sample meal plans to familiarize participants with the DASH dietary pattern (Table 3). We advise them to follow our guidelines for calories, and any discrepancies between our recommendations and those of their tracking devices are discussed during health coach counseling sessions.

2.4.2.6 Energy (calorie) management for intervention women who become pregnant: Health coaches modify calorie goals to keep GWG within current IOM guidelines without compromising diet quality, using a formula developed for the Healthy Moms intervention:[15] Initial Caloric Needs = [(Pre-pregnant weight in kg) (30 kcal/kg/day) (0.70) for women with obesity or (0.85) for women who are overweight] + [(10 kcal) (gestational age in weeks)]. The formula first calculates energy needs based on pre-pregnancy weight using the ACOG factor of 30 kcal/day and reduces that number by 30% for those with BMI ≥ 30 kg/m^2 and by 15% for those with BMIs between 25 and 29.9 kg/m^2 (no reduction for those who achieve a pre-pregnancy BMI < 25 kg/m^2). As pregnancy progresses, we add 10 kcal per week of gestation to accommodate rising basal metabolic rate, thereby tailoring energy goals to gestational age. A woman with a pre-pregnancy weight of 91 kg who is 8 weeks pregnant, for example, is assigned a caloric intake of 1990 kcal/day. The same woman would need 2090 kcal/day at 18 weeks. This calorie prescription resulted in weight gain consistent with IOM guidelines (+0.5 lb/week; range 0.4-0.6) in the Healthy Moms study. Our choice is supported by the American Diabetes Association's suggestion that women with a BMI > 30 kg/m^2 may do well with moderate caloric restriction (30%-33%), particularly if they have gestational diabetes [58].

2.4.2.7 Physical activity goals: Health coaches counsel participants to follow a physical activity plan that can be safely continued into pregnancy, such as walking [59, 60]. According to the American College of Sports Medicine, greater amounts of physical activity are associated with clinically significant weight loss and are important for weight maintenance [61]. We therefore help participants incorporate moderate-intensity physical activity into their lifestyle with the goal of exercising ~60 min most days of the week—whether by performing exercise for short periods several times a day or engaging in one bout of moderate-intensity physical activity. We give intervention participants pedometers and

encourage them to take at least 10,000 steps perday as part of their overall exercise plan. Once pregnant, women are encouraged to discuss their activity level with their obstetricians.

2.4.2.8 Maintenance of weight loss until pregnancy onset: When women reach their pre-pregnancy goal weight, we help them maintain that weight until pregnancy onset, with health coaches offering continued support during their scheduled phone appointments. We use the telephone weight-maintenance intervention followed in the WLM trial and motivational interviewing techniques [34, 42] to help women maintain their diet and physical activity habits and achieve ongoing weight maintenance.

2.5 Participant retention

We keep both intervention and control participants engaged by providing $5 gift cards at the 20-week gestational contact and by sending birthday cards.

3. Outcome measures

We carefully considered the most pragmatic way to collect outcomes given limited resources. We chose to use patient data recorded in the KPNW electronic medical records (EMR). The region's EMR system contains information on health problems, physical findings, tests ordered, medications prescribed, therapies ordered, and progress notes of > 500,000 members. The use of medical record data greatly reduces the cost of data collection and makes it possible to collect data from participants who have difficulty traveling to our location for follow-up data collection. We successfully used this data collection strategy in the Healthy Moms trial, conducted with pregnant women; it showed a high concordance between weights measured in the clinical and research settings [62].

3.1 Primary outcomes, assessment, and rationale

Data are collected from participant EMRs by study staff blinded to randomization status. We document all weights recorded in the EMR of randomized participants and their infants from randomization through the end of data collection. We and others have previously documented the high accuracy of medical record weights in pregnant and non pregnant populations [62-65].

This trial's primary outcome is GWG. In our previous studies of pregnant KPNW patients, we found that pregnant women have frequent physician visits (once in first trimester and then at 16, 20, 22, 28, 32, 36, 38, 40, and 41 weeks of gestation) and are weighed at every visit. We examine GWG from the first prenatal visit to 36 weeks' gestation and calculate whether GWG exceeds current IOM recommendations (which vary based on baseline BMI) [66]. If women do not reach 36 weeks' gestation by the end of study observation, their GWG is adjusted for stage of pregnancy [66]. We also examine weight gain from the first prenatal visit to the routine 5-week-postpartum visit, which occurs between 4 and 6 weeks postpartum. Our previous studies have shown that about 90% of all women delivering babies in KPNW attend the 5-week-postpartum visit within the first 56 days postpartum, where their weight is measured. Postpartum weight measurement allow for exclusion of

contributions of the fetus, placenta, amniotic fluid, and gestational edema from calculations of GWG.

3.2 Secondary outcomes

3.2.1 Weight data—Secondary outcomes include maternal weight at conception. We examine weight at the first-trimester visit as a proxy for weight at conception because most (91%) KPNW women have a first-trimester visit and gain little weight during this time [52]. We also examine offspring birth weight adjusted for gestational age. We obtain birth weights and gestational age from the EMR and adjust birth weight for gestational age [5]. We compute weight for gestational age z-scores using the US natality data set. We have chosen birth weight as a secondary outcome because it is one of the earliest, most easily detectable risk factors of future obesity [67]. We obtain offspring length data from the EMR and calculate weight for length and body mass index z-score using norms developed by the World Health Organization [68]. We recognize there may be some measurement error for newborn lengths, but because these data are recorded in the course of routine medical care, we submit that there is no reason to believe that this measurement error would be different between treatment conditions in this trial.

3.2.2 Participant dietary intake and physical activity—We assess diet via two 24-hour dietary recalls, using the online ASA 24 (http://epi.grants.cancer.gov/asa24/). Outcomes include calorie intake, daily servings of fruits and vegetables, and percentage of energy from saturated fat. Dietary quality measures are based on ACOG and USDA guidelines [55, 69]. We assess physical activity with the Pregnancy Physical Activity Questionnaire (PPAQ), which has been validated in pregnant women [38]. We considered using accelerometers to measure physical activity but did not because of the cost as well as the programming time and equipment required to analyze the data. Another limiting factor in the use of accelerometers or pedometers is the need for users to consistently wear the device, which in our experience would be burdensome to our participants (especially during later stages of pregnancy) and likely result in missing data, especially given the long intervention time (24 months). The outcome variable is minutes of moderate intensity exercise per week. To minimize participant burden, we chose to assess diet and activity at two points, at baseline (preconception) and again at 20 weeks' gestation. We selected 20 weeks because most women no longer suffer from the food aversion and nausea/vomiting of pregnancy, which could affect overall dietary patterns. Reported mean energy intake has shown to be relatively stable from first to second trimester [70].

3.2.3 Feasibility and acceptability—We will examine the feasibility and acceptability of our intervention by measuring call attendance, average call length, and use of the intervention website. At the end of the intervention, women are asked to complete an online questionnaire assessing satisfaction with the intervention, whether they would recommend the intervention to a friend, and how helpful the various parts of the intervention were (website, health coach visits, etc.). Other questions ask about how much and in what way women would be willing to pay for a similar program. In addition, a trained interviewer (separate from the health coach) will conduct semi-structured interviews among a subset of

the population (10%). Selection of intervention participants for interviews will be at random with an oversampling of minority groups.

3.2.4 Additional outcomes—Additional data obtained from the EMR include gestational diabetes screening test results and diagnoses, gestational hypertension, preeclampsia or eclampsia, mode of delivery, delivery complications, and apgar scores of newborn infants. For women who do not get pregnant, we calculate weight change from randomization to the latest recorded weight in EMR at study completion.

3.3 Data analysis plan

When final outcome data become available, we will use an intention-to-treat approach. Prior to conducting the main analyses, we will use chi-square and t-tests to compare the baseline characteristics, including tobacco use, chronic hypertension, and household income, of the intervention and control groups. These variables will be selected for theoretical reasons, such as the effect of tobacco on weight, chronic hypertension on fetal growth, or limited financial resources on access to healthy food. We will use weighted regression to test our primary outcome of GWG closer to IOM recommendations. Weighted regression was selected because follow-up time from randomization until pregnancy varies among women in the study. Weighted regression has been shown to produce robust effect estimates when follow-up time is variable and is not overly sensitive to choice of the weight function [71]. Group assignment (intervention or control) will be the main independent variable. The mother's baseline weight, age, and variables on which the two groups differ will be included in the models as covariates. We will also use weighted regression to test our secondary outcomes of the mother's weight at the first prenatal visit (proxy for weight at conception) and birth weight adjusted for gestational age z score (using US natality norms), controlling for baseline weight and other covariates. We will repeat the analysis excluding women who use reproductive endocrinology interventions. We estimate that too few women will use fertility drugs to allow us to statistically test reproductive endocrinology interventions as moderators or covariates.

3.4 Design limitations and strengths

We are using weights as recorded in the EMR. We carefully considered the best way to collect outcomes given limited resources and our recruitment population of young, busy women [72]. Because we and others have previously documented the high accuracy of EMR-recorded weights in pregnant and non pregnant populations [63-65, 73] and because of the high retention rate in our health system, we feel we can maximize resources by using EMR-recorded weights. We also believe that we can recruit and retain a more diverse population by using EMR instead of requiring follow-up measurements be done in the research center.

Women are in the intervention for variable amounts of time before pregnancy, which means outcomes are collected after variable exposure. Although we adjust for this with statistical modeling, exposure may not differ randomly, as women in the intervention group may have a higher rate of conception and also may become pregnant more quickly as a result of weight loss [29]. However, after implementation of such a program as part of routine care, women

may get pregnant at different times from intervention initiation; therefore, our findings mirror the “real world.”

Our sample size is not large enough to identify significant differences in clinical outcomes with relatively low prevalence such as gestational diabetes or preeclampsia, which is why we focused on weight, diet, and exercise outcomes. A much larger sample would be needed to determine the impact of a pre-pregnancy weight management intervention on such outcomes. However, we are collecting data on these important clinical outcomes and plan to evaluate for between-group differences for powering future studies.

We estimate that about 50% of women will not get pregnant and therefore will not be included in our primary or secondary outcomes. We believe it is imperative to target weight interventions to women considering pregnancy even if they do not get pregnant during our study follow-up. They will still benefit from weight loss and may become pregnant at some point after the study is completed. We hope to conduct in future follow-up studies of this cohort and they could be included in those analyses.

Our study is conducted in an area that is less racially and ethnically diverse than other parts of the US, which could limit the generalizability of our intervention program. Because of this, we are working to over-recruit minority women. After intervention completion, we will specifically recruit minorities for program satisfaction interviews in order to ensure our intervention can be implemented in a diverse population. We will also determine effect sizes by ethnicity and race to examine differences in intervention effectiveness.

Because of limited resources and a desire to decrease participant burden, we are collecting diet and exercise data at only two points (preconception and midway through pregnancy). More data points would have given us a better understanding of dietary changes during the different stages of pregnancy in each group.

Our study has several strengths. We are unaware of any randomized trials of weight loss interventions designed for women pre-pregnancy. Our study may be one of the first trials of its kind to provide information on recruitment, retention, and outcomes for this population. We have designed this trial to appeal to reproductive-aged women. Focus groups with postpartum women have found that they face significant time constraints because of work and childcare commitments, as well as financial issues that may limit their ability to participate [72]. We selected a telephone health coach/website support intervention because it has been shown that postpartum women prefer this approach and it has the highest likelihood of being compatible with reproductive-aged women's lifestyles [72]. Also, a telephone-based intervention appeals to women whose homes are at a distance from clinics that provide in-person sessions, and to women with transportation problems. Our intervention is well suited for dissemination in many types of medical systems because it is conducted primarily through phone calls with a supportive website. Our health coaches are research staff, most of whom are master level trained health counselors and/or registered dieticians, with extensive experience as behavioral health coaches. Because they essentially are functioning as professional behavioral health coaches, their roles could be easily assumed by professional health coaches already working in a health care setting.

4. Conclusion

Prepare is a NIDDK-funded single-center randomized trial of a preconception weight management program utilizing health coaches who maintain individual contact by telephone. The trial aims to improve dietary quality, lower preconception weight, and limit GWG during pregnancy in obese and overweight women. This article reviews several design considerations for the trial that may prove beneficial to future randomized trials. We selected the strategies for their proven efficacy for weight management among non pregnant adults and for their ease of dissemination, should they prove efficacious. Prepare will generate important information about the effects of behavior change strategies begun prior to pregnancy to positively affect both maternal and offspring health. Our study will contribute to the body of research needed to establish appropriate pre-pregnancy counseling advice to overweight and obese women to maximize both their health and the health of their offspring.

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Table 1

Study inclusion/exclusion criteria

Inclusion
Women aged 18-40
Current KPNW members
Expect to be KPNW members for at least 2 more years
Body Mass Index (BMI) ≥ 27 kg/m^2
Not currently pregnant
Access to computer with Internet
Completion of screening diet assessment
English speaking
Exclusion
Taking medication (insulin or pills) for treatment of diabetes
Gastrointestinal disease requiring special diet or medications (for example, ulcerative colitis, celiac sprue, phenylketonuria)
Receiving treatment for cancer
Renal disease (kidney disease requiring special diet or medication)
History of bariatric surgery
Use of prescription weight loss medications in the last 3 months
Another household member already participating in the Prepare study
Answer “no” to the following eligibility interview question: “Would you like to become pregnant in the next 2 years?”
Less than 3 months postpartum

Table 2

Overall intervention goals

Overall goal	Specific instructions
Be an active and engaged participant	Keep your health coach appointments
	Use study website to enter your records
	Set short-term goals and create action plans
Manage calories to be within your customized calorie target	Use a meal pattern guide to help you stay in your calorie target range
	Control portion sizes
	Replace high-calorie foods with lower-calorie options
	Limit sweets and sugar-sweetened beverages
Follow the DASH dietary eating pattern for a healthy diet every day	Eat 8-12 servings of fruits and vegetables
	Eat 3 servings of low-fat dairy
	Limit fat intake (to 25% of calories)
	Aim for 6 small meals and snacks throughout the day
Increase your daily physical activity	Find ways to move more; aim for 10,000 steps
	Exercise daily (gradually work up to 60 min most days of moderate-intensity exercise)
	Follow your doctor's advice and safety recommendations
Keep Records	Weigh yourself at least weekly
	Track everything you eat and drink every day
	Track your exercise every day

Table 3

Sample meal plans.

Meal	1500 kcal	2000 kcal
Breakfast	1 whole grain	2 whole grains
	1 dairy	1 diary
	1 fruit	1 fruit
	1 fat	1 fat
AM Snack	1 vegetable	1 vegetable
		1 protein
Lunch	2 whole grains	2 whole grains
	1 fruit	1 fruit
	2 vegetables	2 vegetables
	2 proteins	3 proteints
	1 fat	2 fats
Aft. Snack	1 dairy	1 dairy
		1 fruit
		1 grain
Dinner	2 whole grains	2 whole grains
	1 fruit	1 fruit
	3 vegetables	3 vegetables
	3 proteins	3 proteins
	1 fat	2 fat
Eve. Snack	1 grain	1 whole grain
	1 dairy	1 dairy