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Predicting Pregnancy in Preconception Weight Loss Trials: Is it Possible?

Jacqueline F. Hayes[1,2] | Suzanne Phelan[3] | Elissa Jelalian[1,2] | Aaron B. Caughey[4] | Kristin Castorino[5] | Casey Heaney[3] | Angelica Mchugh[2] | Rena R. Wing[1,2]

[1]Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University, Providence, Rhode Island, USA | [2]Weight Control and Diabetes Research Center, The Miriam Hospital, Providence, Rhode Island, USA | [3]Department of Kinesiology & Public Health, Center for Health Research, California Polytechnic State University, San Luis Obispo, California, USA | [4]Department of Obstetrics and Gynecology, Oregon Health & Science University, Portland, Oregon, USA | [5]Sansum Diabetes Research Institute, Santa Barbara, California, USA

Correspondence: Jacqueline F. Hayes (Jacqueline_hayes@brown.edu)

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ABSTRACT

Introduction: Predicting pregnancy is a challenge in preconception weight loss intervention trials. The current study examined whether self-reported pregnancy likelihood and timing were predictive of conception.

Methods: Adults (n = 184; 58% Hispanic; age = 33.4 ± 5.1; BMI = 33.6 ± 6.6) with overweight or obesity, prior gestational diabetes mellitus, and plans to become pregnant participated in a pre-conception behavioral weight loss intervention or control. At baseline, participants reported their estimated likelihood of pregnancy from 1 to 10 (categorized as low [1–3], medium [4–7], and high [8–10] likelihood); they also reported expected timeframe for pregnancy.

Results: Over the 4-year trial, 62 (30%) participants became pregnant. Participants who reported a high likelihood of pregnancy were more likely to conceive than those with a lower rating (45.7% vs. 21.1%). The sensitivity and specificity of a high likelihood rating predicting conception were 69%, 95% CI (56.2%, 80.1%), and 58%, 95% CI (48.9%, 67.0%), respectively. Among those who conceived, mean expected time to pregnancy was 21.6 ± 13.2 months while actual mean time was 11.3 ± 9.1 months. Baseline age, ethnicity, parity, BMI, income, and other demographics did not predict conception.

Conclusions: Pregnancy likelihood estimates best predicted conception, but sensitivity and specificity were low. Future work may consider additional ways to screen for likelihood of conception in preconception trials.

1 | Introduction

National recommendations for pregnancy encourage women with obesity to lose weight to reduce the risk of pregnancy complications. These recommendations derive from cohort studies indicating that preconception weight loss can reduce the risk of pregnancy complications [1]. Gestational diabetes mellitus (GDM) is one such complication. GDM is associated with preeclampsia, preterm labor, and cesarean delivery and contributes to long-term risks of type 2 diabetes, cardiovascular disease, and renal disease [2–4]. GDM also poses risks to the infant [2, 4].

Three randomized trials have explored the effects of preconception weight loss on GDM in secondary analyses; however, they have not demonstrated that weight loss prior to conception impacts outcomes [5–7]. The Prepare trial enrolled women planning pregnancy in subsequent 24 months and randomized them to a behavioral weight loss intervention or usual care. In participants who underwent early GDM screening procedures, the intervention group was found to have lower rates of GDM than the usual care group, but group differences were not found in mid-pregnancy [7]. A trial completed by Rönö and colleagues randomized people planning pregnancy to a preconception lifestyle intervention or control; preconception weight losses were not reported and the study did not show any differences in GDM diagnosis in women [5]. Finally, women assigned to preconception standard behavioral weight loss treatment versus a very low energy diet did not show any differences in GDM outcomes despite substantially larger weight losses in women in the VLED condition [6].

Clinical trials assessing weight loss prior to pregnancy face challenges of gaining enough statistical power and timing interventions appropriately; these difficulties stem from accurately predicting whether a person will become pregnant and when conception with occur [8]. Only 30%–60% of participants in existing studies of preconception weight loss interventions actually conceive during the study [5–7, 9]. To gain enough power, significant over-recruitment is required and given the wide variability in pregnancy incidence, identifying an appropriate number of participants is difficult. In women who achieve pregnancy, pregnancy may occur before receiving an adequate intervention dose. For instance, in the trial by Rönö and colleagues, 38% of the intervention group and 52% of the control group only attended one study visit prior to becoming pregnant, limiting the potential impact of the preconception intervention [5]. Another issue is regaining weight following weight loss intervention completion. For many, weight regain begins shortly after intervention completion [10] and even in trials showing good weight loss maintenance, variability in regain is high [11, 12]. The study by Price and colleagues found that the group participating in the standard behavioral weight loss treatment regained approximately 3.0 kg on average in the approximately 1-year follow-up period during the preconception period, which would reverse the 2.1 kg loss [6]. Identification of baseline factors that predict whether an individual will conceive and when conception would occur would aid in reducing over-recruitment burdens and help ensure timely delivery of intervention in preconception weight loss trials.

Inclusion criteria for preconception weight loss trials include intentions or plans to become pregnant in a timeframe relevant to the study. As such, questions designed to assess pregnancy intentions are extremely brief (i.e., one or two items), such that could be completed easily on a phone screen. However, it is clear from the data that not all individuals who respond positively to these screening questions conceive. Assessing the predictive utility of a pregnancy likelihood screening question is useful to inform future trial protocols. Moreover, there may be additional baseline demographics (e.g., married vs. not, using contraceptives) that could be used to help provide insight into the likelihood of pregnancy. The current study examined data from the Gestational Diabetes Prevention/Prevención de la Diabetes Gestacional trial [9] to identify whether a woman's self-reported future pregnancy likelihood predicted pregnancy incidence and timing. The study also examined whether demographic and other baseline variables could be used to predict pregnancy [9]. The overarching goal was to determine if the variables assessed at baseline could predict the likelihood of conception. Such data would be helpful to researchers planning future preconception trials.

2 | Materials and Methods

2.1 | Study Design and Participants

This study is a secondary analysis of a two-site randomized-controlled clinical trial that examined whether a behavioral weight loss intervention delivered before pregnancy reduced GDM recurrence in individuals with overweight/obesity. Women 18 years and older with a previous diagnosis of GDM and a BMI $\geq$ 25 kg/m^2 were recruited from clinics in San Luis Obispo, California and Providence, Rhode Island. Additional inclusion criteria for the parent study included planning to become pregnant in the next 1–3 years and being English or Spanish speaking. The study was approved by relevant Institutional Review Boards and was carried out in accordance with the ethical standards of the 1964 Declaration of Helsinki. Additional details on the methods [13] and outcomes [9] have been published. Participants in the current study additionally had to have provided a future pregnancy likelihood rating of 1–10 using a 0–10 scale (introduced about 1 year after study initiation; ratings of 0 made participants ineligible). No baseline differences in sociodemographic variables were found between participants who provided a likelihood rating (n = 184) and those who did not (n = 15).

2.2 | Interventions

Participants randomized to the standard care plus education condition (Control) received usual care and two 20-min individual sessions with an interventionist, once at baseline and once at 16 weeks. Participants received guidance on how to improve overall health, manage stress and prepare for pregnancy. Participants randomized to the weight loss intervention received all aspects of the Control condition and additionally received a behavioral weight loss intervention designed to produce a 10% weight loss over 16 weeks and then weight loss maintenance until conception [13].

2.3 | Measures

Assessments were completed at baseline and pregnancy incidence and timing were tracked throughout the 5-year trial.

Anthropometrics. Weight was measured using a calibrated standard digital scale to the nearest 0.1 kg, and height was measured in millimeters using a wall-mounted stadiometer.

Demographics and pregnancy history. A self-reported demographic questionnaire assessed age, race, ethnicity, income,

education, and marital status. Participants were also asked about the number of previous pregnancies and whether they were currently using hormonal birth control or an intrauterine device.

Pregnancy Likelihood and Timing Rating. At screening, participants responded to the question "On a scale of 0–10, what are the chances you see yourself ever having more children?". A response of one or higher was needed to be eligible. Participants were then asked to estimate their timeframe for future pregnancy in an open-ended manner. If a single estimate (e.g., 2 years) was provided, this was used for analysis and if a range was provided (e.g., 1–2 years), the midpoint was used for analysis. Pregnancy accuracy was defined as predicting pregnancy within ± 6 months of actual pregnancy. If conception occurred in this window, the estimate was considered accurate.

Pregnancy Incidence. Pregnancy incidence and timing were tracked across the study.

2.4 | Analysis

Descriptives for continuous variables are presented as means and standard deviations and categorical variables are presented with *n*'s and percentages. Pregnancy likelihood ratings were looked at both continuously and categorically (low: 1–3, medium: 4-7, high: 8–10; low and medium categories were combined for statistical analysis due to low *n*'s). Pearson correlations between likelihood rating and pregnancy as well as between estimates of timing until pregnancy and actual pregnancy timing were calculated. Prior work reported no significant differences in pregnancy incidence by randomized group [9]. Logistic regressions, controlling for group assignment, were used to examine additional baseline predictors of pregnancy incidence in (1) the whole sample and (2) individuals who provided high (8–10) likelihood ratings at baseline. Baseline predictors assessed were BMI, age, number of previous pregnancies, birth control usage/type, marital status, employment, education, and Hispanic ethnicity.

TABLE 1 | Baseline characteristics of participants in the gestational diabetes prevention trial.

Characteristic	Total $n = 205$
Age, years, mean (SD)	33.4 (5.1)
Hispanic/Latino, no. (%)	119 (58.0)
Heritage, no. (%) (participants could select multiple)	
American Indian or Alaskan native	3 (1.5)
Asian	10 (4.9)
Black or African American	11 (5.4)
Native Hawaiian or Pacific Islander	2 (1.0)
White	27 (42.9)
Other	87 (42.4)
Married; no. (%)	153 (74.6)
Annual household income $, no. (%)	
< $50,000	107 (52.2)
≥ $50,000	97 (47.3)
Education, no. (%)	
High school or less	85 (41.5)
Some college/college or more	120 (58.5)
Employment, no. (%)	
Employed full time (at least 35 h.wk)	74 (36.1)
Employed part time (less than 35 h.wk)	46 (22.4)
Unemployed	85 (41.5)
Prior pregnancies, mean (SD)	2.6 (1.5)
Contraceptives	
Hormonal (including hormonal IUD)	53 (26.4)
Non-hormonal IUD	12 (5.9)
BMI, kg/m^2, at study entry, mean (SD)	33.6 (6.6)
Weight status	
Overweight, no. (%)	71 (34.6)
Obese, no. (%)	132 (64.4)

3 | Results

Participant demographics are presented in Table 1. Sixty-two participants became pregnant over the trial with a mean timing of 11.3 ± 9.1 months. Approximately half (51.0%; $n = 94$) of women enrolled in the study rated their likelihood of becoming pregnant to be high (rating 8–10), 37.5% indicated a medium likelihood rating (rating 4–7; $n = 69$), and 11.4% indicated a low likelihood rating (1–3; $n = 21$). The median likelihood rating was 8 and the most common responses were 5 and 10 (Figure 1). Women who indicated a high likelihood rating of pregnancy at baseline were significantly more likely to become pregnant across the course of the study ($n = 43$, 45.7%) than those with a lower likelihood rating (1–7; $n = 19$, 21.1%), $X^2(1,1) = 12.49$, $p < 0.001$. The correlation between likelihood rating and pregnancy was $r(183) = 0.272$, $p < 0.001$. The sensitivity and specificity of a high likelihood rating predicting pregnancy incidence were 69.4%, 95% CI (56.2%, 80.1%) and 58.2%, 95% CI (48.9%, 67.0%), respectively. Figure 1 shows pregnancy incidence by baseline likelihood rating.

Among women who became pregnant, there was a trend-level correlation indicating that women who had a higher pregnancy likelihood rating were likely to get pregnant earlier in the study timeline ($r = -0.23$, $p = 0.091$). Only 15 of the participants who became pregnant (26%) did so between 5 and 12 months, the ideal pregnancy timing for the study to receive the full intervention but limit regain. The median likelihood rating of women who did become pregnant in 5–12 months was 10 with a mean (SD) of 8.7 (2.1) (Table 2). Women who became pregnant in 0–4 months ($n = 18$) had a median likelihood rating of 8.5 and a mean likelihood rating of 7.8 (2.3) and women who became pregnant in the following year (months 13–24, $n = 20$) had a median likelihood rating of 10 and a mean of 9.1 (1.3) (Table 2). Participants ($n = 147$) estimated they would become pregnant in an average of 1.8 ± 1.1 years. Of those with timing estimates who became pregnant ($n = 44$), 31.8% ($n = 14$)

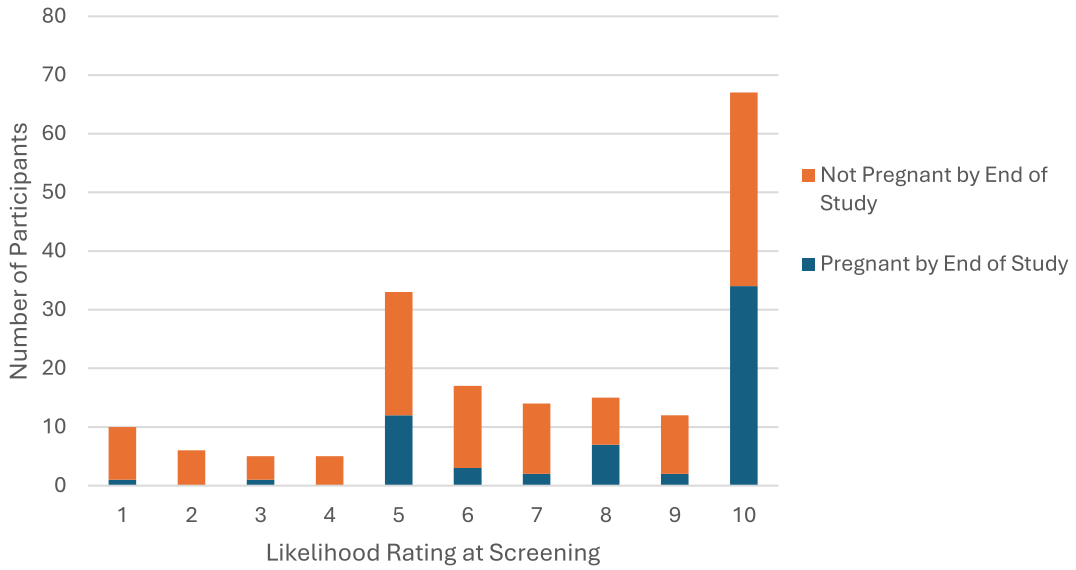

FIGURE 1 | Frequency of pregnancy likelihood estimate at baseline by pregnancy incidence at the conclusion of the study.

TABLE 2 | Median and mean likelihood of pregnancy ratings by timing of participant conception.

Pregnancy timing	*N*	Median likelihood rating	Mean likelihood rating
0–4 months	18	8.5	7.8 ± 2.3
5–12 months	15	10	8.7 ± 2.1
13–24 months	20	10	9.1 ± 1.3
25+ months	4	4	3.5 ± 1.9

predicted their timeframe accurately (± 6 months of prediction), whereas 56.8% ($n = 25$) conceived earlier than expected and 11.4% ($n = 5$) conceived later than expected.

None of the baseline factors tested were significantly associated with pregnancy incidence in the full sample. Results were also not significant when looking just at individuals who indicated a high likelihood of future pregnancy at baseline; however, marital status ($B = 0.94$; $p = 0.08$) and Hispanic ethnicity ($B = 0.78$; $p = 0.072$) approached significance with results indicating that married and non-Hispanic women were potentially more likely to become pregnant.

4 | Discussion

Asking women to rate the likelihood that they would conceive was the best predictor of the actual outcome in the current study. Women who rated the likelihood of becoming pregnant as high were more likely to become pregnant than women who indicated a lower likelihood. A high likelihood rating could thus be used as enrollment criteria. However, only about 50% of women who rated their likelihood as high became pregnant, and the sensitivity and specificity of this screening measure were relatively poor.

A similar question to the pregnancy likelihood question asked in the current study is the "One Key Question", which is "Would you like to become pregnant in the next year?" and allows for responses of "Yes", "No", "I Don't Know" or "I'm Okay Either Way" [14]. Though this has been explored in clinical contexts, little data on its predictive nature exists. A version of the One Key Question adapted to a 2-year timeframe was utilized in the Prepare trial [7], which excluded individuals who responded "No". The Prepare trial had a pregnancy rate of 51.8%, similar to what was found in the current trial for individuals with a high likelihood rating.

Other, more detailed self-report measures exist, such as the Desire to Avoid Pregnancy scale (DAP) [15]; however, as the name implies, it was developed to assess a preference to avoid becoming pregnant. Additionally, the DAP has 14-items that ask relatively sensitive questions (e.g., "Becoming pregnant in the next 3 months would bring me closer to my main partner"; "If I had a baby in the next year, it would be hard for me to manage raising a child") and is thus not as easily administered as an initial screening tool. Nevertheless, predictive modeling suggests that only enrolling individuals with a DAP cut-point of 0.5 or lower (on a scale of 0–4) would lead to a pregnancy incidence rate of 72.7% over 12 months, which is substantially higher than the current trial [16]. Though the DAP was published after recruitment for the current trial began, a pragmatic pathway to potentially improve pregnancy incidence rates in preconception trials could be to ask a one-item question, such as the one assessed in the current study or the One Key Question during initial screening procedures, and provide the DAP as a secondary screening measure. Future preconception trials may consider this two-pronged approach.

Predicting pregnancy timing was even more of a challenge; less than a third of the participants predicted their timeframe

accurately (± 6 months of prediction). Accuracy in reporting pregnancy timing is helpful in the context of a preconception weight loss trial to ensure that participants receive the full intervention protocol and the chances of regaining weight following active intervention are minimized. In this study, participants tended to overestimate the time to pregnancy. Unintended pregnancies are common; in 2011, unintended pregnancies accounted for 45% of total pregnancies in the United States [17]. Thus, it is possible that participants who overestimated their timeline were not explicitly trying to conceive when they became pregnant. Participants were encouraged to refrain from becoming pregnant prior to intensive intervention conclusion; however, no explicit counseling around preventing pregnancy occurred. Inclusion of counseling to employ birth control measures up to the conclusion of the intervention may be useful for ensuring that participants receive a full intervention dose prior to becoming pregnant.

Aside from the pregnancy likelihood question, no other baseline variables assessed were associated with pregnancy incidence in this sample of individuals who had a previous pregnancy and were considering becoming pregnant again. However, in individuals already endorsing a high likelihood of pregnancy, there were statistical trends to suggest that those who were married or non-Hispanic white were more likely to become pregnant during the study's 1–3 years time frame. Further research is needed to develop an algorithm that integrates a variety of variables to support pregnancy prediction in diverse populations at high risk of diabetes.

This study has limitations. The number of participants who became pregnant was small, which limits the ability to find predictors of this outcome. Moreover, a substantial number of patients were using contraceptives at baseline. It is unclear how contraceptives played a role over time in conception, but is worth consideration in future preconception trials. An additional limitation is that the pregnancy likelihood rating scale is not validated and was not used in the full sample from the parent trial. Finally, the results should be interpreted in consideration of the eligibility criteria for the study, namely women who had GDM diagnoses in previous pregnancies. Different results may be found in a broader sample of women potentially considering pregnancy.

In conclusion, recruiting for preconception weight loss trials is challenging given the difficulty in predicting the incidence and timing of pregnancy. Assessing the likelihood of becoming pregnant was the only predictor of conception, though only half of the individuals who rated their pregnancy likelihood as "high" actually conceived. Further work on a screening process to increase pregnancy incidence in preconception trials is needed. Including a brief screening item and a longer, more detailed follow-up questionnaire may be a practical solution to increase conception rates, though this remains to be tested.

Author Contributions

J.F.H., S.P., and R.R.W. conceived and designed the research and helped draft the manuscript. K.C., A.B.C., R.R.W., E.J., S.P., C.H., and A.M. participated in the design and coordination of the study and data acquisition methods and helped draft the manuscript. E.J., S.P., R.R.W., C.H., and A.M. participated in the design and development of the intervention. J.F.H. completed the statistical analysis. C.H. and A.M. participated in the design of the visits. All authors read and approved the final manuscript.

Conflicts of Interest

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