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Reducing sexual health risks and substance use in the prenatal setting: A study protocol for a randomized controlled trial

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ABSTRACT

Sexually transmitted infections (STIs) are at a record high in the United States, and STI risk is a critical and costly public health concern for childbearing women. STIs can lead to a number of serious health risks including premature birth, low birth weight, ectopic pregnancy, and fetal death. Similarly, there has been a dramatic increase in substance use during pregnancy, leading to complications during pregnancy and poorer birth outcomes. Women who misuse substances are disproportionately more likely to engage in risky sexual behaviors that can result in STIs. The proposed study will test whether the Health Check-Up for Expectant Moms (HCEM), a computer-delivered brief intervention that simultaneously targets STI risk and alcohol/illicit drug use during pregnancy, reduces antenatal and postpartum risk more than an attention, time, and information matched control condition among pregnant women seeking prenatal care. The study is a two-group, randomized controlled trial in which a diverse sample of 250 pregnant women will be recruited from prenatal care clinics and assigned to either (a) a computer-delivered, single-session brief intervention plus two booster sessions); or (b) a computer-delivered control condition. Follow-up assessments will occur at 2 and 6 months from baseline, and at 6 weeks postpartum. Our objective measures include STI incidence and birth outcomes. The results of this trial will fill a critical gap and provide much-needed data on the efficacy, costs, and resource utilization of a practical computer-delivered, brief motivational intervention tailored to reach high-risk women during pregnancy and extending impact to postpartum.

1. Introduction

Sexually transmitted infections (STIs), alcohol, and drug use during pregnancy are common and critical interrelated factors that are associated with negative consequences for the mother, fetus, and infant. STIs are an urgent concern for childbearing women [1], especially for pregnant women who can transmit the infections to their babies. National STI prevalence rates are rising, particularly among childbearing women, and nearly 25% of pregnant women are infected with one of four STIs [2]. Between 2016 and 2017, national rates of syphilis among women increased by 21%, and by a staggering 44% among newborns [3]. Adverse effects of prenatal STIs can include miscarriage, stillbirth, low birth weight, and neurological injury. Drug use also has major health consequences for the pregnant women that can in turn negatively affect fetal development, rates of STIs, depression, intimate partner violence, as well as significant complications. Recent reviews suggest infants whose mothers used marijuana during pregnancy, compared to those who did not, were more likely to have lower birth weights, increased risk of preterm birth, and require neonatal intensive care [4–6]. Prenatal alcohol exposure can lead to a wide range of adverse effects, known as Fetal Alcohol Spectrum Disorders (FASD) with an estimated 12,000 infants born with FAS each year, and up to three times as many have alcohol-related problems [7].

In national survey data from 2017, past month prevalence of all drug use was 8.5% for pregnant women [8]. There has been a dramatic national five-fold increase in opiate use during pregnancy [9], leading to a surge in the incidence of neonatal abstinence syndrome (NAS) of 383% over the past decade [10]. Marijuana use during pregnancy is also on the rise [11], increasing by 62% over the past decade. Nearly 12% of pregnant women

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reported using marijuana in the past year, in part due to an increased perception of the safety of marijuana use during pregnancy [12,13]. The legalization of marijuana for medical and recreational purposes, along with approved cannabis use for nausea in some states, may be a contributing factor to the increased use during pregnancy [14]. Twenty-four percent of women in their first trimester of pregnancy report using alcohol, and nearly 13% report past-month binge drinking (4 or more drinks in a row) [8]. The use of alcohol/drugs increases the probability for sex risk behavior through disinhibition and impairment of judgment [15,16], making the case for addressing these behavior risks together.

There are currently no brief interventions that target both of these risks simultaneously during pregnancy. A recent study identified alcohol use as a critical factor in reducing sex risk behaviors, suggesting the importance of implementing this target in STI preventive interventions, however, it excluded pregnant women [17,18]. Recent meta-analysis has indicated the superiority of targeting multiple health behaviors rather than just focusing on one behavior [19–21].

Despite the escalating rates of both risks among pregnant adult women, very few STI-focused interventions have specifically targeted the antepartum period and there are currently no brief interventions that target risky sexual behaviors and alcohol/drug use simultaneously to address the unique needs of pregnant women, including health risks to the fetus. The proposed project will test an innovative and low-cost computer-delivered intervention, *Health Check-Up for Expectant Moms* (*HCEM)*, which is theoretically driven and will address unique barriers in early intervention with at-risk women throughout pregnancy, including the challenges of disclosing highly stigmatizing behaviors [22], with the effects hopefully extending into the postpartum period. A fully powered trial of the HCEM optimized to extend impact to the postpartum period is necessary to determine efficacy.

2. Methods

2.1. Study aims

Aim 1: To test the overall hypothesis that HCEM, compared to an attention, time and information matched control condition, will reduce risk of STIs and alcohol/illicit drug use among at-risk pregnant women during pregnancy at 2 and 6-months follow-up. The specific hypotheses to be tested are:

(a) HCEM, as compared to control, will result in fewer unprotected sexual occasions;
(b) HCEM, as compared to control, will result in lower alcohol use and illicit drug use, and fewer heavy episodic drinking days.

Aim 2: To test the hypothesis that HCEM will be associated with key secondary outcomes. Specifically, we postulate.

(a) HCEM, as compared to control, will result in fewer STIs (re-infection and/or new infections) during pregnancy and at 6-weeks postpartum;
(b) HCEM, as compared to control, will result in fewer unprotected sexual occasions and lower alcohol use and illicit drug use at 6-weeks postpartum;
(c) HCEM, as compared to control, will result in less adverse birth outcomes (e.g., low birth weight).
(d) To collect and measure resource utilization and costs of HCEM to provide preliminary data to assess feasibility for future implementation and dissemination and to inform practice guidelines.

Aim 3: To explore direct and indirect effects in the above hypotheses:

(a) To explore the effect of HCEM on the intermediate outcomes of pregnancy-specific knowledge and risk perceptions, autonomous motivation and self-efficacy during pregnancy;
(b) To test these immediate outcomes as potential mediators of HCEM primary effects hypothesized above.

2.2. Approach

The proposed study is a two-group, randomized, controlled design with an initial session (conducted close to the first prenatal visit), plus two booster sessions within one month later (at 2 and 4 weeks). There will be follow up assessments at 2 and 6 months from baseline encounter, and at 6 weeks postpartum, conducted by computer and delivered by the research assistant either at the clinic or at participants' home. Birth outcome (e.g., gestational age, birth weight, APGAR score) data will be obtained by post-delivery review of birth records. We will focus on testing the efficacy and utility of the theoretically driven HCEM to target STI risk during pregnancy and postpartum, integrating alcohol and illicit drug use given the well-supported relationship between these risks. The proposed study will use a sophisticated intervention development tool, the Computerized Intervention Authoring Software (CIAS) [23–25]. A technology-delivered intervention approach promotes scientific rigor and greatly facilitates replicability in the community.

2.3. Preliminary data from R21

The research team conducted an RCT pilot study of 50 high-risk pregnant women attending prenatal care in a large urban clinic in Providence, RI, with comparable patient demographics to the clinical sites proposed in the current study. The intervention received very high mean ratings of satisfaction (6.3 out of 7), and the computer software was rated highly by both control and the intervention participants (4.6 out of 5). Feedback from the exit interview was positive with participants consistently reporting that they found the intervention educational, interesting, and realistic. The RCT was feasible in terms of recruitment and enrollment of participants. A total of 401 women were screened over the course of nine months, with 34% meeting eligibility criteria. Of the 50 women enrolled for the randomized trial, all 50 completed an interaction session with the computer, which was either the intervention or a control condition. Within one month of the interactive session, all participants were asked to return to the study site where they completed a 15-min, computer-delivered booster session of the same conditions as before. Forty-nine women (98%) completed the booster session and assessment 4 months later, demonstrating feasibility and uptake of these sessions. Participants in the HCEM condition demonstrated a significantly larger reduction in any self-reported marijuana or alcohol use compared to control condition (time-by-group interaction $p = .015$). Formal statistical tests from the results of STI testing (for trichomoniases) were not performed due to limited amount of data. There was a higher reduction of unprotected sex at follow-up in the intervention arm than control (27% vs. 5%); the direction and magnitude of this effect was very promising and would be of clinical significance, however, was not significant with this small sample size ($p = .12$); see Fig. 1, above) [21]. The lack of significance regarding unprotected sex reduction may also indicate that additional contact may be needed for our high-risk group of pregnant women, supporting a second booster session in the proposed trial.

The Health Check-up for Expectant Moms (HCEM) (see Fig. 2, below) is a brief intervention (one session plus two booster sessions) that is derived from empirical support, using motivational interviewing (MI) and informed by the Information- Motivation-Behavior (IMB) model [26], which are both found to be effective for STI/HIV risk reduction. MI [27,28] is an intervention approach with wide dissemination and demonstrated efficacy [29,30]. Consistent with the Self Determination Theory (SDT) [31], MI is a client-centered counseling style that facilitates internal motivation to change through alignment of behavior change with deeply held beliefs, values, and goals. MI utilizes evolving readiness and self-efficacy to change. Moreover, the MI model appears to be generalizable to different populations, including low-income urban women [32–35]. The components of the STI and alcohol/illicit

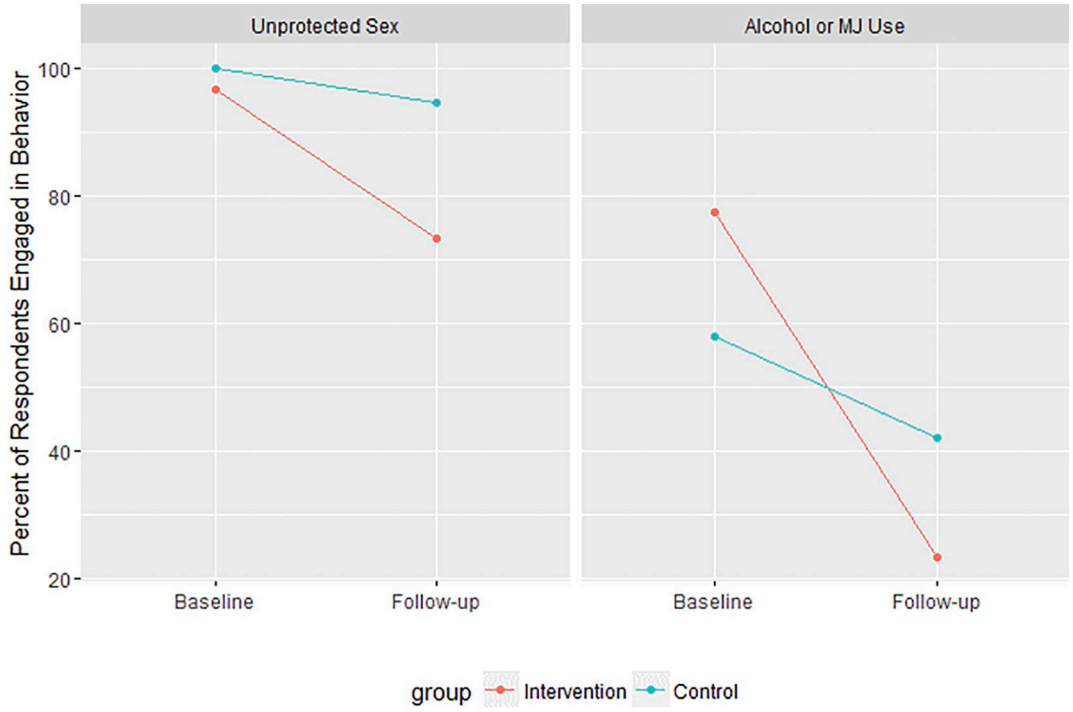

Fig. 1. Reductions in Main Outcomes of R21 Study.

drug use risk reduction to be used in HCEM are formulated to be highly specific to the perinatal setting and entail increasing knowledge and targeting risk perceptions about STI transmission and prevention during pregnancy, increasing intrinsic motivation to act during pregnancy based on that knowledge, and ensuring sufficient behavioral skills (self-efficacy) to change behavior (e.g., increase in condom use, decrease in substance use) during pregnancy, as self-efficacy can be a strong predictor of condom use in women [36]. Such an MI-based, STI risk reduction intervention, may be of particular value for pregnant women at risk for alcohol/illicit drug use in reducing STI risk, because MI identifies these women' strengths and builds upon their successes (i.e., other changes they have made during pregnancy), thereby countering experiences and perceptions that may make them vulnerable for substance use. Additionally, MI with its collaborative and non-confrontational approach and its emphasis on increasing awareness to successful steps towards their well-being is consistent with recommendations for brief interventions in substance use, including increasing self-efficacy and relapse prevention skill sets to extend into postpartum [37].

HCEM begins with an Information/Advice component, which provides facts about STI transmission and prevention, associated risks of alcohol and drug use for both woman and fetus, and highlights the bidirectional relationships among these risk factors. HCEM includes testimonial videos of women who had an STI and/or used substances during pregnancy. Participants are taught male and female condom application with anatomical models as the literature suggests that skill-building interventions improve self-efficacy in condom use among high-risk females [38]. Participants have the option to choose which specific drug(s) she would like to focus on and provides opportunities for her to practice behavioral skills to reduce risks (e.g., negotiation communication of their intentions to partners). HCEM emphasizes the interconnected risk factors of risky sexual behavior and alcohol/drug use and provides opportunities for change and goal-setting [38].

Within one month of completing the intervention, participants in both conditions will complete two, 15–20-min booster sessions delivered remotely. For participants in the control condition, the booster content will be similar to the baseline content. For participants in the HCEM condition, the booster sessions will review their own personalized change plan and identify any challenges or barriers to increasing safety behaviors (i.e., intention to increase condom use and/or reduction of the substance that they selected). Review of the personalized change plan will include: reduction in STI risk behavior, including alcohol/illicit drug use, and identification of triggers for unsafe sex.

3. Participants and procedures

We will enroll 250 pregnant women (as close as possible to first prenatal visit), age 18 or older, and will follow similar recruitment to the R21 study given feasibility and acceptability rates. Specifically, the

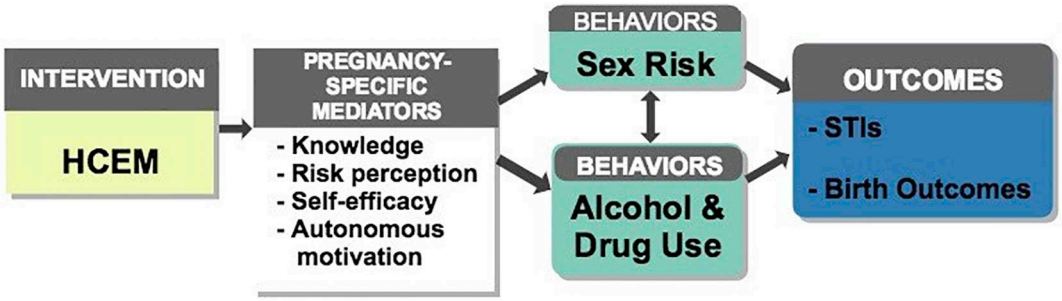

Fig. 2. Conceptual Model of HCEM Effects and Mechanisms.

Table 1
Study measures.

		Antenatal		Postpartum
Self-report measures	Baseline	8 weeks	24 weeks	6 weeks
Demographic information	X			
Marlowe-crowne social desirability – short form [42]	X			
Timeline follow-back, sex, alcohol, illicit drug use [43]	X	X	X	X
Condom use self-efficacy [36]	X	X	X	X
Treatment self-regulation questionnaire [44]	X	X	X	X
STI knowledge questionnaire [45]	X	X	X	X
Risk perceptions items (STI)	X	X	X	X
Importance, readiness, and confidence rulers [46,47]	X	X	X	X
Condom attitude scale [48]	X	X	X	X
Perceived competence scale [49]	X	X	X	X
Objective biometric measures				
Urine collection: STI testing (X), STI & drug testing (XX)	X	XX	X	XX
Birth outcomes				X
Hair sample testing	X		X	
Economic and implementation measures				
Direct costs (hardware, software)	X	X	X	X
Time costs (time required by clinic staff)	X			
Time costs (time required by patients)				X

study will include pregnant women who endorse: 1) at least one unprotected vaginal (or anal) sex occasion (USO) in the past 30 days (supported by the literature for our "high risk" sample, identified as such based on childbearing age, urban, ethnically diverse, and reporting co-morbid recent history of substance use [38,39], and 2) current alcohol/illicit drug use risk, based on self-reported measures of current or previous use [40,41]. Exclusion criteria include: 1) inability to provide informed consent (e.g., clear cognitive impairment), or 2) inability to understand English. The study protocol has been reviewed and approved by the University of Michigan Medical Institutional Review Board (HUM00143896) and is registered on ClinicalTrials.gov (NCT03826342).

The clinical trial will be conducted at high volume prenatal obstetrics and family medicine clinics that are sites of a University health system. We chose these clinics because they provide access to socioeconomically, racial/ethnically, culturally diverse pregnant patient population. Potential participants will be approached in a number of ways, including direct contact with a study staff member prior to their appointment in the waiting room and being informed of the study by clinic staff. Those who express any interest in the screening survey will be directed to speak with the study research assistant (RA) to complete the short (10-min) computer-delivered health survey including questions to determine eligibility. The computerized screening will use the CIAS software delivered on an easy to use iPad. The screener will include well-validated and recommended measures of risk behaviors for this population [40,41]. The research team has used this procedure successfully to recruit this target population.

Women who score eligible on the screener will be informed by the RA about the clinical trial and will explain and obtain the informed consent. The baseline session (60 min) will be conducted in a private room in the clinic, providing a confidential and comfortable environment for the participant. Upon completion of the baseline session, and following previous studies with similar design, [23] women in both study conditions will receive appropriate referrals for: (1) testing and treatment for STIs, and (2) a Centers for Disease Control and Prevention (CDC) brochure specifically designed to facilitate reductions in drinking and illicit drug use during pregnancy. Additionally, all participants in this study will receive care as usual from their medical team; no screening, referral, or counseling will be withheld in any way at any time. The computer program will randomize participants to either the HCEM intervention condition or control condition. Participants can receive up to $205 for study completion.

Booster sessions can be completed at participants' home (or clinic, if preferred) and accessed through our secure, HIPAA-compliant study website using either a computer or mobile device. Assessments will be completed at the clinic and scheduled with prenatal visits. The postpartum assessment will be conducted by the RA at a private and confidential location convenient to the participant (e.g., clinic, home), coordinated with the timing of the postpartum medical visit, maximizing likelihood of completion.

We will use the same, well-validated, attention, time and information-matched control used successfully in our five previous studies with pregnant women, [23,24] including in the pilot R21 (ratings of acceptability were equally high among intervention and control group participants). The content will consist of a series of questions regarding television show preferences and viewing a brief series of videos of popular entertainers/shows, with subsequent requests for ratings of subjective preference. We will include facts about alcohol, drug use, and risky sex during pregnancy, along with informational brochures from the CDC that provide face validity.

3.1. Assessment measures

We will collect measures of our primary, secondary, and tertiary outcomes (Table 1). All self-reported measures included in this study have good psychometric properties. Birth outcome data (e.g., gestational age, birth weight, NICU admissions) will be available to the team by accessing patient medical records postpartum.

3.2. Data analysis

Descriptive statistics will be calculated to summarize baseline characteristics for the full cohort and compared between arm using *t*-tests and chi-square tests. Any identified confounders with $p \leq .10$ will be included in all subsequent analyses. The Timeline Follow-back will determine frequency outcomes through the number of days in the 90-day period that the participant is engaged in a risky behavior. This will be carried out separately for each of the outcomes.

Aim 1, Hypotheses (a) and (b): The outcomes of interest are the number of days (of the 90) of unprotected sex, drug use, and alcohol use. We will also explore the differences in the number of heavy episodic drinking days although the prevalence of this was extremely low in the pilot data. The outcomes will be analyzed under a clustered count regression framework (Poisson or Negative Binomial) with frequency of the behavior as outcome, and time (baseline, 2 months, 6 months), group (HCEM, control) and time-by-group interaction as the primary covariates. A generalized linear mixed models (GLIMMIX) approach will be adopted assigning a random subject intercept to account for the clustering within each participant. The regression model will be further controlled for potential confounders such as demographic characteristics and other variables that are identified to be significantly associated with outcome in the univariate analyses. Changes over time within each group will be estimated post-hoc by sliced effects derived from the regression model. In additional analysis, reduction in proportion of participants engaged in the risky behavior on ≥ 1 days within the 90-day period will be analyzed using a clustered logistic regression with a dichotomous outcome at the subject level indicating the status of the engagement, and with time (baseline, 2 months, 6 months), group (HCEM, control), time-by-group interaction as the primary factors. In order to control for the potential Type I error inflation due to multiple testing, we will use $p = .01$ as the threshold for significance.

Aim 2, Hypotheses (a) and (b): In order to compare the frequency of STIs and unprotected sexual occasions at 6-week postpartum between

Table 2
Parameters used in power simulation.

Outcome	Baseline mean	F/U-Intervention mean	F/U-Control mean
Sex[a]	35.6	29.0	31.4
Alcohol	4.52	0.25	0.63
Drug	17.96	2.26	0.67

[a] Random effect variance was estimated to be 1.75 for sex model, alcohol and drug use had very low within subject correlation so no random effects were used in power simulations for those outcomes.

HCEM and control arm, we employ a count regression model framework as in Aim 1. These will be cross-sectional models with the 6-week postpartum values as dependent variables and group as the primary factor. The models will be controlled for the corresponding baseline values as well as all the potential cofounders.

Adverse birth outcomes, such as low birth weight will be considered as a dichotomous variable and will be compared across the study arms under a logistic regression framework.

Aim 3, Hypotheses (a) and (b): We will use a structural equation modeling (SEM) approach. These will include pregnancy-specific measures of autonomous motivation, self-efficacy, knowledge and risk perceptions (Table 1). These measures are all continuous and will be measured at all three time points. All relevant direct and indirect effects will be evaluated. Significance of the indirect effect of the mediators will be tested using bootstrap method which appears to have good power in small samples [50].

3.3. Costs

HCEM costs will be measured using a micro-costing approach [51]. Summary statistics for total direct HCEM-specific costs will be reported. Additional component cost outcomes will be reported including implementation time for clinic staff and patient time for completing the initial brief intervention and booster sessions. Net costs (savings) will be calculated by subtracting mean direct costs per participant in the control arm from mean costs per participant for HCEM. The primary outcome for the cost analysis will be expressed in dollars per STI positive event averted (Hypothesis 2d). Secondary cost outcomes will include clinic staff time, patient time, and start-up costs.

3.4. Power

We estimated power based on our R21 study and calculated it using extensive simulation. We considered the difference between baseline and at 6-months in number of days of unprotected sex, alcohol and drug use for power calculations. Power was obtained under a Poisson regression framework with time, group, and time-by-group interaction as covariates. Data was generated 1000 times from models characterized by time and group specific means as well as the variance of the random effects estimated from the pilot data. Various parameters used in the simulation are indicated in Table 2. Power was assessed for the interaction term as well as the main effects empirically by the proportion of times the corresponding coefficient was deemed statistically significant at 5% level. For all the outcomes, our proposed sample of 250 should be adequate for detecting small to moderate effect sizes. Specifically, in the pilot data we saw an overall average baseline number of days of unprotected sex of 36 with a drop to 32 and 29 in the control and HCEM groups, respectively. Using 100 subjects per arm, the difference in this reduction will be deemed as statistically significant with > 90% power. The power for alcohol and drug use was > 95% using the parameters in Table 2. Allowing for a 20% drop-out, we plan on recruiting 125 participants per arm yielding a total of 250.

3.5. Assessment of factors affecting implementation

We will explore factors that affect integration of HCEM into primary care. We will interview approximately six staff stakeholders (e.g., clinical staff including nurse, social worker) at each site to assess perceived barriers and facilitators, workflow impact, and fit with patient and site needs. [Using a Likert Scale (1–5), providers will be asked questions about the feasibility and clinical utility of HCEM (e.g., "Will HCEM improve the overall quality of perinatal care?; "What is the likelihood of incorporating HCEM into your prenatal program?").

4. Discussion

HCEM is the first brief intervention that simultaneously targets two significant and prevalent health risks, STIs and alcohol/drug use, that has been structured to address the unique needs of pregnant women. With the alarming increases nationally in both STI rates and drug use among women, there is a clear need for an intervention tailored to these unique needs of this vulnerable population. Because the majority (97%) of pregnant women receive at least some prenatal care, [52,53] the CDC and ACOG have identified the perinatal period as an urgent time for STI prevention and subsequent behavior change, including substance use, to reduce risk for acquiring infection [54]. The proposed project will test an innovative, high-reach, easily implementable, low-cost computer-delivered intervention that is theoretically driven and will address known barriers in early intervention with at-risk women throughout pregnancy and will hopefully extend intervention effects into the postpartum period. A fully powered trial of HCEM optimized to extend impact to the postpartum period is necessary to determine efficacy.

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