Comparing the Effectiveness of Clinicians and Paraprofessionals to Reduce Disparities in Perinatal Depression: Protocol for a Cluster-Randomized Controlled Trial

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Abstract

Background: Postpartum depression is highly prevalent in low-income women and has significant health and mental health effects on mother and child. Home visiting (HV) programs provide services to large numbers of perinatal women in the United States and are a unique and potentially powerful setting for delivering mental health services for women experiencing depression. Although there are interventions that reduce the risk of developing postpartum depression among low-income women, none have used non-health or non-mental health professionals as interventionists.

Objective: This paper outlines the protocol and recruitment process of a cluster randomized trial funded by the Patient-Centered Outcomes Research Institute (PCORI) that evaluates whether the Mothers and Babies (MB) group intervention, when led by paraprofessional home visitors, is more efficacious than usual care. It will also examine if MB, when led by paraprofessional home visitors, is not inferior to MB delivered by mental health professionals (MHP). MB has previously demonstrated efficacy when delivered by MHP and pilot work indicated promising results using paraprofessional home visitors to deliver the intervention.

Methods: A cluster randomized trial is being conducted with 38 HV programs. Sixteen HV programs will deliver MB using MHP, 16 will deliver MB using paraprofessional home visitors, and six will deliver usual HV services. We anticipate recruiting 933 women ≥ 16 years old enrolled in HV programs who are ≤ 33 weeks’ gestation and speak either English or Spanish. Women in the two intervention arms will receive the six-session MB group intervention. Baseline, post-intervention, 12-week postpartum, and 24-week postpartum assessments will be conducted to assess client outcomes. Semi-structured interviews will be conducted with approximately 30 home visitors and 25 MHP who serve as group facilitators and 90 study participants to gain qualitative data on intervention successes and challenges. Analyses will proceed at the participant level. Primary analyses for depressive symptoms score at 24 weeks postpartum will involve a linear mixed model, controlling for baseline symptoms and other covariates, and random effects to account for clustering.

Results: We have recruited 730 women through the end of June 2018. Recruitment will be completed at the end of September 2018.

Conclusions: There is considerable potential to disseminate MB to HV programs throughout the United States. Should our results demonstrate home visitor efficacy when compared to usual care and/or non-inferiority between paraprofessional home visitors and MHP in improving mental health and quality of life outcomes, no additional financial resources would be required for existing HV staff to implement MB. Should this study determine that home visitors are less effective than MHP, we will generate more wide-scale evidence on MB effectiveness when led by MHP.

Trial Registration: ClinicalTrials.gov Identifier: NCT02979444

Keywords: Perinatal Depression; Prevention; Pregnancy; Randomized Controlled Trial; Home Visiting
Introduction

Background
Postpartum depression is a serious mental health disorder that poses significant health and mental health risks for mothers and their infants [1]. Research suggests that prevalence rates of postpartum depression are higher among low-income women than among middle- or high-income women [2,3]. There is also consistent evidence that low-income women are less likely to receive mental health services in the perinatal (i.e., pregnancy until child’s first birthday) period than their more affluent counterparts due to a variety of factors, including stigma related to mental health service use and lack of access to community-based mental health providers [4,5]. Postpartum depression is a particularly serious problem for low-income women. It is estimated that over 10% of infants from low-income households have a mother who has major depression and more than 50% have a mother with some depressive symptoms [6]. Postpartum depression also has negative consequences for maternal parenting practices. Compared to women not suffering from postpartum depression, depressed women tend to be less positive, less spontaneous, and less responsive with their infants [7]. Postpartum depression has been linked to developmental delays among infants of depressed mothers, including social interaction difficulties, attachment insecurity, and cognitive impairments [8,9].

Systematic reviews have highlighted an array of efficacious interventions that reduce the risk of developing postpartum depression [10]. Among those interventions that have demonstrated efficacy, the majority use health (e.g., nurses, midwives) or mental health (e.g., psychologists) professionals to deliver individualized or group-based interventions (see Dennis & Dowswell, 2013 for a review). One exception is the use of peers to deliver peer support via phone [11], although this study was conducted in Canada with predominately White, upper and middle class women. As such, there are no interventions led by non-health or non-mental health professionals that have demonstrated efficacy in preventing the onset of postpartum depression and reduction of depressive symptoms among low-income women.

Home visiting (HV) programs that provide services to perinatal women are one of the largest avenues through which perinatal women come to the attention of service providers, making HV a unique and viable setting for delivering mental health services. Although professional HV models exist (e.g., Nurse-Family Partnership), most HV programs in the United States use paraprofessional home visitors, who lack formal training in the helping professions [12]. This study was born out of HV programs’ need and desire for a low-cost intervention that could prevent the onset and worsening of depression among the population they enroll. Maternal depression is an enormous challenge facing HV programs, with an estimated 10-15% of HV clients exhibiting major depressive disorder and another 45-50% exhibiting subthreshold depressive symptoms [13]. Furthermore, there is consistent evidence that low-income women exhibiting depressive symptoms—including women enrolled in HV programs—do not access mental health treatment in the community [4]. Lack of available mental health professionals, stigma in seeking mental health services, and logistical challenges (e.g., childcare, transportation) are a few of the barriers low-income women face when seeking mental health services. For those clients who do access services, most perinatal women are likely to receive pharmacological treatments [14], despite the fact that the vast majority of perinatal women prefer non-pharmacologic interventions [5]. HV programs are ideal settings for delivering mental health care to perinatal women because their mission is not stigmatizing and HV programs tend to be trusted entities in the communities they serve.

Prior Work
Previously, study investigators established the efficacy of a group-based intervention—Mothers and Babies (MB)—in preventing the onset of postpartum depression and reducing depressive symptoms when led by mental health professionals in a group setting [15-17]. Based on these randomized controlled trials (RCTs), Health Research and Services Administration has recommended HV programs use the MB group intervention in addressing and preventing maternal depression. MB is also listed on the Substance Abuse and Mental Health Services Administration Evidence-Based Program Registry [18]. Subsequently, the Principal Investigator (PI) and colleagues worked closely with HV clients, staff, and other key stakeholders to develop training and
implementation protocols to facilitate implementation of the MB group model by paraprofessional home visitors. In particular, training protocols and instructor manuals were modified to provide greater clarity on key aspects of MB’s cognitive-behavioral underpinnings. Results from a pilot study with two HV programs in Baltimore indicated that women receiving the MB group intervention delivered by paraprofessional home visitors showed improvements in depressive symptoms, suggesting that the MB intervention could be delivered by home visitors instead of mental health professionals. This project builds on this preliminary work, by evaluating the effectiveness of the MB group model when delivered by paraprofessional home visitors.

Goals of the Study

This study is a cluster-randomized controlled trial in which HV clients receive either a) MB delivered by mental health professionals, b) MB delivered by paraprofessional home visitors, or c) usual HV services. There are four specific aims:

1. Evaluate efficacy of MB delivered by paraprofessional home visitors in comparison to usual care (i.e., HV without MB) on patient-reported outcomes, including depressive symptoms, quality of life, parenting practices, engagement in pleasant activities, and relationship with one’s partner.
2. Assuming efficacy in #1, assess non-inferiority (NI) of MB delivered by paraprofessionals versus mental health professionals.
3. Explore patient characteristics as potential covariates and/or effect modifiers.
4. Examine the feasibility and acceptability of MB delivered by paraprofessional home visitors and mental health professionals.

Methods

Study Sites

HV programs in Illinois, Ohio, Minnesota, Missouri, Michigan, Iowa, and West Virginia who indicated the ability to recruit approximately 40 pregnant women over a 16-18 month timeframe were recruited to participate in the study. All HV programs recruit women at high risk for poor pregnancy and/or parenting outcomes via referrals from prenatal care clinics, community outreach, and current program participation. Forty-five HV programs agreed to participate in the study. We staggered the start of implementation among the programs so that only a subset of the program sites were beginning to implement at one time.

Randomization

The study employed a modified covariate-constrained randomization [19] design at the HV program level, using unequal (1:3:3; control: mental health professional delivery of MB: paraprofessional delivery of MB) allocation, with intention to achieve relative balance in a set of pre-specified program-level potential covariates. There are three variables for which we chose to control imbalance at the study site level at baseline through this approach:

1. Percent non-White clients as reported by the site (treated as a continuous variable)
2. Site yearly client volume (also reported by site and treated as a continuous variable)
3. Population density of the site area (continuous variable)

The covariate-constrained method of randomization allows for efficient balance of multiple covariates at once and is recommended over other methods (i.e., simple randomization or matching) for cluster-randomized trials. The general procedure involves:

1. Enumerating a large subset of possible allocation schemes.
2. Evaluating (im)balance for each variable of interest (in this case we have three) for each possible allocation.
3. If the (im)balance is acceptable according to some pre-specified criterion, then we save this scheme in a smaller subset of potential allocations for implementation.
4. Of those that meet acceptable levels of imbalance, we randomly select one allocation for use in the current study.

We chose the p-value corresponding to the Kruskal-Wallis test as our criterion for ‘balance’ in step #3 above. If the p-value for each of the three variables is larger than 0.30 for a given simulated allocation scheme, that particular allocation is deemed ‘acceptable’. This criterion is adapted from the ‘Minimal Sufficient Balance’ principle from Zhao et al. [20] in the individual sequential randomization literature.

Randomization occurred in three waves for logistical purposes. The first included 14 sites (2 C:6 MH:6 HV); the second included 19 sites (4 C:7 MH:8 HV); allocation ratio was slightly off in this wave to account for dropout sites); and the third wave included 12 sites (1 C:6 MH:5 HV). Thus, we randomized a total of 45 sites in three waves.

After randomization, seven programs dropped out, thereby yielding a total of 38 active study sites; six of these sites removed themselves prior to implementing the intervention and one after beginning implementation and enrolling participants. Data collected from all study participants will be used in the analysis. Among the 38 active study sites, 16 HV programs are receiving the MB intervention delivered by mental health professionals, 16 are receiving MB intervention delivered by HV paraprofessionals, and six programs serve as control sites and are not implementing the MB intervention.

**Intervention Delivery**

The MB Group curriculum is six sessions, with each session designed to last 90-120 minutes. The curriculum consists of three modules that map onto key components of cognitive behavioral therapy (CBT): pleasant activities, thoughts, and contact with others. The first part of each module teaches participants to understand how a given component influences their mood. Subsequently, participants receive concrete skills related to each module. These skills provide participants with a “toolkit” of skills they can use to improve their mood. We refer to each six-session MB group as a cohort. Each cohort meets weekly for six consecutive weeks at the HV program site, with occasional groups skipping a week due to inclement weather or holidays. Light refreshments are provided at each session. Transportation to the sessions and child care supports are also provided for participants, if necessary. All MB sessions are audio-recorded using a portable device for purposes of examining intervention fidelity. The study design called for random selection of 20% of these audio sessions to be assessed and coded for fidelity. The group facilitator transfers the recordings to Northwestern University Research team within 24 hours of each individual session using a secure Northwestern University Box account. At the end of June 2018, 98 cohorts were completed. Implementation of all prenatal MB cohorts will be completed by October 2018.

**Interventionist Training and Supervision**

We have trained 105 paraprofessional (Bachelor’s degree or less) home visitors and supervisors from 16 program sites that are using home visitors to deliver the MB intervention. Of the 105 home visitors trained, to date, 33 have delivered the intervention. We have also trained 32 mental health professionals (MHP) from the 16 intervention sites using MHP to deliver MB; 21 of these MHP have delivered the intervention. MHP for the purposes of this study are Masters-level professionals in the areas of Child and Family Studies, Psychology, Psychiatry, Social Work, or a related field with a minimum of five years’ experience working with families and young children. These MHP live and work in the states in which they deliver the intervention, and either the participating HV programs or a state professional association (e.g., The Illinois Association for Infant Mental Health) recruited them.
The study PI led MB trainings, consisting of 8-12 contact hours, for home visitors and mental health professionals. The PI conducted a total of 19 trainings in the seven participating states. All of the trainings maintained the same contact hours with trainees but were delivered in three formats; in-person, webinar, and telephone. Home visiting supervisors from each of the HV programs (irrespective of study arm) also attended the training. The MB training covers: the conceptual underpinnings of MB (e.g., its cognitive-behavioral framework); a brief history of previous implementation of the MB Program with diverse perinatal populations; instruction on the format of the MB instructor manual; and instruction on how to maximize the use of the group format when delivering MB. Training includes discussion of each MB session from start to finish. Training is interactive with opportunities for discussion and modeling communication of material by the PI. Training also involves group activities, where training attendees practice delivering curriculum material and receive extensive feedback on strengths and areas needing improvement from the trainer and other training participants.

Home visitors and MHP receive phone supervision from the PI the first time they deliver MB. During these supervision sessions, the PI first debriefs the completed MB session and then helps the facilitator plan for the subsequent group session. For home visitors who continue to facilitate groups, the HV program manager assumes the supervisory role—with support from the research team. Along with support from the PI during supervision, MHP and paraprofessional home visitors can share and receive feedback via the study ListServ which includes other HV staff, MHP, home-visiting supervisors, and the research team.

**Study Participants**

Our recruitment goal for the C-RCT is 933 pregnant women. The 38 HV programs participating in this project enroll clients via referrals from prenatal care clinics, Women, Infants, and Children (WIC) programs, and other settings working with pregnant women. HV programs implementing MB groups will implement an average of five MB cohorts, over the course of the project. Women ≥ 16 years old enrolled in HV programs who are ≤ 33 weeks’ gestation and speak either English or Spanish are eligible for enrollment. Women are not excluded based on race/ethnicity or based on demographic characteristics other than the ability to speak English or Spanish.

**Recruitment and Informed Consent**

Women meeting eligibility criteria for the C-RCT are approached by HV staff who explain the MB intervention and research study. Interested women complete a referral form with the HV staff and are informed that a study Northwestern University Research Assistant (RA) will contact them with more information about the research study. HV staff send the referral forms to the NU research team via e-mail or fax. RAs share responsibility for calling referred women to explain the study in more detail and complete the informed consent process with eligible participants who indicate interest in study participation.

The Northwestern University Institutional Review Board (IRB) granted a waiver of written documentation of consent, allowing online informed consent via REDCap [21], or consent via telephone for potential participants without easy access to web-based resources. If the referred participant meets eligibility criteria and is interested in participating in the study, the RA indicates that a web-link with instruction on completing the baseline assessment via REDCap will be emailed or texted to them.

Participants are informed via informed consent and during all assessments that they may choose to not answer any question at any time for any reason and that not answering questions will not affect their relationship with their HV programs or ability to keep receiving the MB intervention (for those enrolled in the two intervention arms). Both the online consent form and the study surveys are available in English and Spanish. Each time a study participant fills out a survey, the survey includes a prompt to the participant asking if they wish to continue her participation by completing the next survey.

A waiver of parent permission was granted in order to waive the signature of parents of children who are
participants (pregnant women ≥ 16 years old and < 18 years old). This research involves minimal risk to the participants by only requiring the administration of online surveys and/or telephone interviews to collect data. Guidance from the U.S. Department of Health and Human Services Office of Research Protections (OHRP) indicates that individuals < 18 years of age can consent to study participation without parental consent if the study procedures for which they are consenting are such that they could provide consent outside of the research context.

Prior to beginning group facilitation, all facilitators receive a web-based informed consent form via REDCap (Research Electronic Data Capture) [21] that they must complete prior to their first group session. In addition to the consent, facilitators are asked to complete a brief demographics questionnaire prior to facilitating groups and a survey inquiring about supervision support they receive after facilitating each cohort. All consented MHP and home visitors who facilitated a MB cohort are eligible to participate in a semi-structured interview. The Intervention Coordinator approaches them after they have completed facilitation of their last MB cohort. Northwestern University’s IRB approved all recruitment and consent procedures.

Data Collection Procedures and Study Assessments

The study includes four data collection time points—baseline, immediately post-intervention (or eight weeks after the baseline for control participants), 12 weeks postpartum, and 24 weeks postpartum. Participants will receive $20 remuneration after completing the baseline, 12-week and 24-week assessments for a total of $60. Baseline and follow-up data will be collected and managed using REDCap. Baseline data will be collected within 2-3 weeks of establishing client eligibility and participation agreement. Women who do not complete the web-based baseline assessment in this timeframe will be contacted by phone by the RA to complete the assessment by phone, ensuring that baseline data are collected prior to the first MB group.

Table 1 describes the study’s outcome indicators, measures, and data collection time points. This study’s primary outcome is reduction in depressive symptoms with several secondary outcomes (e.g., behavioral activation, mood regulation) that are closely linked with MB content.

Table 1. Study outcome indicators, measures, and data collection time points

<table>
<thead>
<tr>
<th>Outcome Indicator</th>
<th>Measure</th>
<th>Baseline</th>
<th>Post-Intervention</th>
<th>12 weeks postpartum</th>
<th>24 weeks postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>Quick Inventory of Depressive Symptomatology (QIDS-SR16)[22]</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Secondary Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>Edinburgh Postpartum Depression Scale[23]</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behavioral Activation</td>
<td>Behavioral Activation Depression Scale[25]</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Pleasant Activities</td>
<td>Pleasant Activities Schedule[26]</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Mood Regulation</td>
<td>Negative Mood</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
We are collecting data on MB acceptability via three data modalities. First, we are conducting brief semi-structured interviews with 90 intervention participants—45 who received MB led by MHP and 45 who received MB led by paraprofessional home visitors. Second, we are conducting brief semi-structured interviews with all home visitors and MHP who deliver MB. Third, all participants will complete brief paper and pencil checklists immediately after receiving an MB session. Group facilitators will collect these checklists. We ask each intervention participant to rate each session using three questions used in previous MB studies: “how much did you enjoy today’s group session?”, “how well did you understand what we talked about during today’s group session?”, and “how often do you think you will use the skills and information that you were given during today’s group session?”

**Retention Strategies**

Recruitment procedures emphasize the importance of participating in all MB sessions and remaining in the study through the 24-week postpartum assessment. The research team obtains ample tracking information at baseline which includes the participants’ name, email address, home and cell phone numbers, mailing address, HV site, and secondary contacts indicated by the participant. The research team updates contact information and each participant’s preferred mode of communication (e.g., phone, text, Facebook) at each follow-up assessment. We allow participants without easy access to the internet and/or those less comfortable completing surveys electronically to complete follow-up surveys by phone. We conduct intensive follow-up with participants throughout the study via monthly communication from the RAs using the participant’s preferred modes of contact. We follow all study participants through the 24-week postpartum assessment regardless of their attendance at intervention sessions or completion of previous assessments.

**Data Monitoring Plan**

The Intervention Coordinator refers any study participant who endorses thoughts of self-harm on the QIDS-SR16, EPDS, or MMS to the HV program supervisor. The supervisor uses his/her agency’s protocol to make a determination necessary steps to ensure the safety of the study participant. The research team notifies the PI and Research Project Manager immediately of any such referrals. In addition, should a participant indicate experience of severe depressive symptoms upon completion of a depression scale assessment, study staff notify the supervisor at the HV program in order to provide appropriate referrals for their client’s mental health treatment linkage. In addition to following up with the HV supervisor, RAs also follow-up with study participants to ensure they are not in immediate danger of harming themselves and provide a list of resources to the participant. The statistical team, in collaboration with the rest of the study team, developed a series of data
status and quality reports via an automated task, which study staff review multiple times per week. They include: participant status, missing survey and overall data, mood assessment summaries, and intervention adherence reports.

**Statistical Analysis**

**Outcomes**

Primary outcome of interest for Aims #1-#3 will be the Quick Inventory or Depressive Symptoms (QIDS-SR16) score as determined by participant self-report at 24 weeks postpartum. We will control for baseline QIDS-SR16 score, and treat this measure as a continuous variable. It ranges from zero to 27 points, where higher scores signify increased depressive symptoms. QIDS-SR16 translates into depressive categories such that a score of less than five points indicates no depression, a score ranging from six to 10 indicates mild depression, 11-15 signifies moderate depression, 16-20 indicates severe depression, and anything above 20 would be labeled as very severe [22]. As a result, we deem a five-unit change or difference in score to be meaningful (as a jump in five points would result in an increase in depression severity tier for any individual patient). Secondary outcomes will address key components of the MB intervention. They include: incidence of major/clinical depression, behavioral activation, engagement in pleasant activities, mood regulation, social support, decentering, perceived stress, responsive parenting, and relationship with partner, and subjective well-being.

**Statistical Methods**

Descriptive statistics will summarize baseline characteristics (both site-level and participant-level) overall and by arm. As appropriate, mean ± standard deviation (or median [inner quartile range] will be used in cases of skewed or non-normal empirical distributions) and frequency (proportions) will summarize continuous and categorical data, respectively. Analyses will employ normal theory methodology as appropriate, and in cases of violations of assumptions, transformations and/or nonparametric analyses may be utilized.

Analyses will proceed at the participant level. Primary analyses for QIDS-SR16 score at 24 weeks postpartum will involve a linear mixed model for continuous outcome with independent variables of baseline QIDS-SR16, study arm (three-level factor), and site-level baseline covariates used in randomization algorithm. We plan to account for clustering effects via inclusion of a random site effect, which will allow for distinction of between and within-site variance. Intra-cluster correlation coefficients will be estimated via variance components estimates. Intervention effect will first be evaluated via the adjusted Wald type III test for significant study arm effect at the 5% level of significance. If arm is significant at the 5% level, analyses evaluating the superiority (Aim #1) of HV-led intervention vs. control will proceed with Tukey’s correction for multiple pairwise hypothesis tests. Assuming the Tukey-adjusted p-value for this comparison falls below the 5% level of significance in favor of the HV-led arm, we will further assess the non-inferiority (Aim #2) via pairwise comparison (using Tukey’s correction) of adjusted 24-month QIDS in HV-led vs. MH-led arms. Figure 1 below depicts the margin and zone of non-inferiority for this comparison.
Figure 1. Margin of Non-inferiority (NI)
The double-sided arrows represent 95% confidence intervals for the model-estimated adjusted mean 24-week difference in QIDS-SR16 score between arms. Note that higher score signifies more depressive symptoms; thus if the estimated difference (HV minus MHP score) is larger than zero, the HV arm has on average worse depressive symptoms. Since the pre-specified margin of non-inferiority is two units on the QIDS-SR16 scale, we will claim NI if the upper limit of the adjusted 95% confidence interval for the paraprofessional home visitor-led arm minus the MHP-led arm comparison remains below two. The red arrows indicate scenarios in which we cannot claim NI and the blue arrows indicate scenarios in which the criterion for non-inferiority is met.

Using the same analytic approach, we will add covariate-by-arm interaction terms in the aforementioned model to explore whether effectiveness of intervention varies by patient characteristics (Aim #3). The covariates to be explored include: race/ethnicity, first-time mother, geographic type of HV program (urban, suburban, rural). These analyses are more exploratory in nature, and thus power/sample size considerations do not focus on interaction effects. As a result, we anticipate evaluating interaction effects at the 10% level of significance without adjustment for multiple hypothesis tests. Qualitative data analysis methods will evaluate feasibility and acceptability of MB in each setting (Aim #4), and the details of these analyses will be specified elsewhere.

Additional analyses surrounding Aims #1-#3 will employ longitudinal methods, utilizing all study data at all time points (i.e., inclusion of a fixed study time point effect). Secondary outcomes will all be analyzed in this fashion with the exception being binary response variables (e.g., depression onset). In these cases, models will involve appropriate link and distributional assumptions (logit, binomial, respectively). For the participants receiving active intervention (either paraprofessional home visitor-led or MHP-led MB), we will examine a ‘dose’ variable in relation to outcomes. This dose variable will be defined as the number of sessions (out of six possible) attended for an individual participant.

We plan to conduct analyses on the modified intent-to-treat (mITT) dataset whereby all participants randomized with data at the 24-week postpartum time point will be analyzed according to arm to which they were allocated. We will further perform a sensitivity analysis on the ‘as treated’ dataset. Those in either active intervention arm will be considered ‘treated’ if they attend at least four out of the six sessions required for the MB course.
Power and sample size considerations allowed for some missing data and, as specified in our approved research plan, we have allowed for entire clusters to drop out of each arm; however, in the event of large amounts of missing data (i.e., more than 15%), we will explore multiple imputation analyses. We will examine rates of missing data for all variables and determine whether the rates vary by participant characteristics, HV program location, or intervention arm. These summarizations will inform potential biases resulting from missing data. The mixed effects models planned for analyses are generally robust for unbalanced data across study time points. If multiple imputation methods are merited, we will impute at least five datasets to generate an estimated average intervention effect. These analyses will again serve as sensitivity analyses to the previously outlined analyses.

**Power and Sample Size Considerations**

As in any C-RCT, power and sample size considerations depend heavily on intra-cluster correlation coefficient (ICC) estimates. In general, it is recommended that these calculations account for anticipated ICC as failure to do so in the design phase and lead to an increase in type II error (i.e., result in underpowered studies) [34,35]. Without previous knowledge of ICC(s) in this population with respect to our primary outcome, we explored a range of ICCs (0.001 to 0.05). Power calculations assume a standard deviation in primary outcome of approximately six points (on the QIDS-SR16), with a meaningful difference corresponding to five points on average across arms. Thus, for the superiority aim, we calculated power based on the average ability to detect at least a five-point mean difference between control sites and paraprofessional home visitor-led sites. Power calculations assumed a 5%/3 = 1.7% level of significance in order to account for three pairwise comparisons. This is an approach that we deem conservative as this mirrors the Bonferroni correction for multiple hypothesis tests.

We have 38 active sites: six control, 16 paraprofessional home visitor-led sites, and 16 MHP-led sites. We plan to recruit an average of 27 participants per site, allowing for up to 15% attrition (i.e., 23 participants on average for analyses). These assumptions allow for more than 95% power to detect a mean difference of five points in QIDS-SR16 across arms for an ICC of 0.01. Even if one of the six sites drops out, and if ICC is as large as 0.05 (which we deem unlikely), we still anticipate over 85% power for analyses addressing the efficacy aim (Aim #1).

Power for the NI aim will require ability to detect a smaller (margin of NI of two points) mean difference across arms. We anticipate over 90% power to detect a margin of NI of two points on the QIDS-SR16 scale if we assume an ICC of 0.01 and 16 sites in each of the intervention arms with 23 participants for analyses, on average, per site. This allows for up to 15% attrition overall. We anticipate some sites to be over/underperforming and thus unequal representation per site is inevitable. Our hope is that the precautions taken with respect to the randomization algorithm that attempts to control imbalance in yearly volume and population density will offset biases created by over/underrepresentation for participants at specific sites. While we do not anticipate ICC to be larger than 0.01, we present the required sample size per site in Table 2 below in order to ensure 90% power under the same assumptions for all scenarios explored. We also present sample size requirements in the event that one of the active sites drops out in each of the intervention arms (i.e., 15 sites per arm). Notice that if ICC is larger than 0.02 (which we are not anticipating, although it remains possible), our projected sample size does not allow for 90% power in this case. Since these assumptions are all rather conservative, we argue adequate power for detection of both superiority and non-inferiority. Power calculations for assessment of heterogeneity of intervention effects depending on participant characteristics (Aim #3) require even more assumptions for which we have little information. Thus, we do not necessarily anticipate power to detect specific effects within subgroups or power to detect interaction effects, but we plan to use the analyses outlined here to explore these effects.
Table 2. Required sample size for 90% power in non-inferiority aim

<table>
<thead>
<tr>
<th>ICC</th>
<th>N HV sites</th>
<th>N MH Sites</th>
<th>N per site for analyses</th>
<th>N recruited per site (allowing for 15% attrition)</th>
</tr>
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<tbody>
<tr>
<td>0.001</td>
<td>16</td>
<td>16</td>
<td>17</td>
<td>20</td>
</tr>
<tr>
<td>0.01</td>
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**Results**

This study is in progress. Recruitment for this C-RCT commenced in January 2017 and we anticipate enrollment will continue through September 2018. Through the end of June 2018, we have enrolled 730 women into the study. We have completed qualitative interviews with five home visitors and six mental health professionals who have delivered MB cohorts who will not be facilitating future cohorts, and 55 participants who have received the intervention.

**Discussion**

**Comparison with Prior Work and Future Possibilities**

This study integrates a low-cost intervention into HV programs, some of which are being infused with new federal funding through the Affordable Care Act. These HV programs serve large numbers of perinatal women at-risk for major depression whom existing mental health services often overlook. Should we find that women receiving MB from paraprofessional home visitors exhibit a) better mental health outcomes than women receiving usual care and/or b) similar improvements to women receiving MB from mental health professionals, there is considerable potential to expand this intervention to HV programs across the country. This is feasible since home visitors are already employed at the setting in which the intervention occurs, thus minimizing the need to procure additional, potentially costly, resources. No previous studies have demonstrated efficacy in preventing the onset of postpartum depression among low-income women using interventions led by non-health or non-mental health professionals. As such, this study will also advance the field of postpartum depression prevention.
This research also allows for the delivery of mental health services outside the public mental health system. The difficulties of paying for prevention and early intervention are well documented, as most health plans require a diagnostic code for billing and do not reimburse for prevention of mental illness including depression. The novel integration of a depression prevention intervention into HV programs provides a potential avenue for delivering depression prevention to women at increased risk for developing major depression in the postpartum period.

**Conclusions**

We feel that this study is likely to increase patient engagement in HV programs. As such, study participants will not only see improvements in their own mental health, but are likely to experience greater benefit from the services and supports provided by HV programs aimed at improving positive parenting behaviors, increasing linkages with prenatal and postpartum care, and increasing the use of child preventive healthcare services (e.g. timely well-child visits). Thus, we believe that this study has important implications for improving maternal and child health in multiple domains during the perinatal period.

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*Author Contributions*

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JJ is the Research Project Manager on the RCT and was a major contributor in writing the manuscript
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AD is the Research Coordinator on the RCT and was a major contributor in writing the manuscript
MS is the Implementation Coordinator on the RCT and was a contributor in writing the manuscript
AD is the Research Assistant on the RCT and was a contributor in writing the manuscript
JS is the Research Assistant on the RCT and was a contributor in writing the manuscript
DT is the Principal Investigator for the RCT and was a major contributor in writing the manuscript

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*Conflicts of Interest*

None declared
Abbreviations

CBPR: Community-based participatory research
CBT: Cognitive Behavioral Therapy
EPDS: Edinburgh Postnatal Depression Scale
HV: Home visiting
ICC: Intracluster correlation coefficient
MB: Mothers and Babies
MDD: Major Depressive Disorder
MHP: Mental Health Professionals
MMS: Maternal Mood Screener
NI: Non-inferiority
PI: Principal Investigator
QIDS-SR16: Quick Inventory of Depressive Symptomatology Self-Report
RA: Research Assistant
RCT: Randomized controlled trial
REDCap: Research Electronic Data Capture

References


