Title:	**The Social Media-Based Parenting Program for Women with Postpartum Depressive Symptoms**
Short Title	The Parenting with Depression Study
Drug or Device Name(s):	N/A
Regulatory Sponsor:	National Institutes of Health (NIH)
eIRB Number	19-016174
Protocol Date:	12/2/2020
Amendment 1 Date:	Amendment 3 Date:
Amendment 2 Date:	Amendment 4 Date:

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ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse event
PSI-SF	The Parenting Stress Index-Short Form
PSOC	The Parenting Sense of Competence Scale
PCERA	Parent-Child Early Relational Assessment
MSPSS	Multi-dimensional Scale of Perceived Social Support
EPDS	Edinburgh Postpartum Depression Scale
NCS	National Comorbidity Survey
PPD	Postpartum Depression
TFI-8	Therapeutic Factors Inventory-8
BDI-II	Beck Depression Inventory-II

ABSTRACT

Context: (Background)

Our long-term goal is to develop effective parenting strategies to facilitate optimal child development for mothers suffering with PPD symptoms. Our overall objective for this application is to study whether this program combined with online depression treatment leads to more responsive parenting (target) and signals improved child language, socioemotional and cognitive development (outcomes) compared to depression treatment alone.

Objectives: (primary and important secondary objectives)

1. To determine whether a social media-based parenting program can improve responsive parenting (target) among mothers with PPD symptoms.

    a. Hypothesis 1: Mothers who participate in the parenting program will demonstrate greater improvement in responsive parenting than those who receive online depression treatment alone.

Study Design:

A prospective, randomized comparative group treatment trial to determine whether the social media-based parenting program can improve responsive parenting among women with PPD symptoms.

Setting/Participants:

The proposed study will occur at up to 6 primary care practices (initially starting at 3-4) affiliated with a large urban children's hospital (The Children's Hospital of Philadelphia).

In the first phase, 75 ethnically and racially diverse mother-child dyads will be recruited who screen positive for PPD symptoms (EPDS score>9) at their child's well visit and have infants < 8 months of age.

Study Interventions and Measures:

Participants will be randomized to receive the parenting program plus online depression treatment or online depression treatment alone to assess target engagement.

The results of this application would be expected to contribute important new knowledge and inform a future trial on parenting strategies to better assist mothers with PPD symptoms and improve child developmental outcomes.

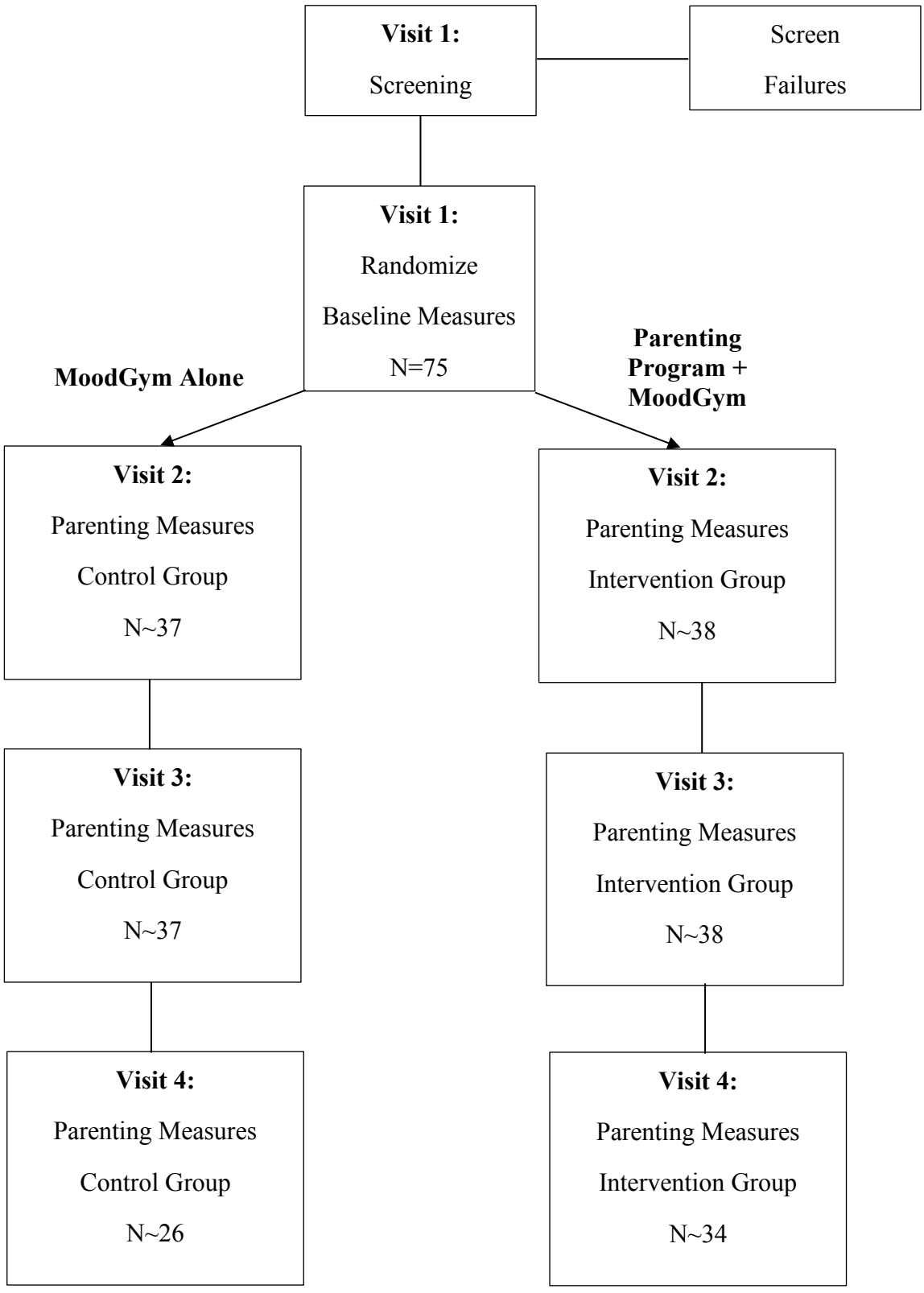
TABLE 1: SCHEDULE OF STUDY PROCEDURES[1]

Study Phase	Month 0	Month 1	Month 2	Month 3[2]
Visit Number	**1**	**2**	**3**	**4**
Informed Consent	X			
Randomization	X			
Demographics	X			
PSI-SF	X			X
PSOC	X			X
PCERA	X			X
MSPSS	X			
Poverty	X			
BDI-II	X			X
EPDS	X	X	X	X
NCS Item		X	X	X
MoodGym Acceptability Survey				X
TFI-8				X (Intervention arm only)
Acceptability Survey				X (Intervention arm only)
Parenting Program		X (Intervention arm only)	X (Intervention arm only)	
MoodGym		X	X	

[1]All visits may be conducted either in-person or remotely

[2]As necessary, Visit 4 may occur as late as Month 6

FIGURE 1: STUDY DIAGRAM



1 BACKGROUND INFORMATION AND RATIONALE

Postpartum depression (PPD) is prevalent following the birth of a child, occurring in 12-24% of women.[1-4] Depressive symptoms are relatively uncommon among women prior to puberty, rise markedly during a woman's childbearing ages, and then fall during older adulthood.[5] For example in a study among women of childbearing ages 24 to 44 years old, 19% endorsed depressive symptoms compared with 8% of older women.[6] Young mothers are particularly vulnerable to depression; studies report varying prevalence rates of 12% to 50% among mothers of young children.[7-11] The occurrence of depression following the birth of a child has a strong genetic component,[12-14] is likely related to the stress of childbirth and parenting, and may be related to hormonal fluctuations during the postpartum period.[7,9] Environmental stressors such as poverty and social isolation also contribute additional risk to the development of depression following childbirth.[7,15-17]

PPD symptoms adversely impact responsive parenting, i.e. a mother's ability to nurture and care for her children.[18,19,20,21]Depressed mothers lack knowledge of and self-efficacy in healthy parenting practices, e.g. recommended sleep practices for infants.[22-24] They are less likely to display positive parenting behaviors, e.g. delivering praise, and more likely to endorse negative parenting behaviors, e.g. yelling and spanking, than non-depressed mothers.[24-26] In addition, depressed mothers ineffectively model emotional expression, which may contribute to emotional dysregulation and higher stress levels in infants and children.[27,28] Overall, the literature suggests that depression adversely affects the mother-child relationship, leads to less responsive parenting, and contributes to disorganized infant attachment with mothers.[29-31]

As a result of these maladaptive parenting behaviors, infants and toddlers may experience cognitive, language, and socioemotional delays as early as 12-18 months of age.[28,32-35] Affected children are also at greater risk to develop behavioral problems by age three than children of non-depressed caregivers.[18,28,30,31,34,36] These behavioral problems encompass both internalizing disorders such as anxiety and depression and externalizing disorders including oppositional-defiant disorder and conduct disorder. The longer, persistent, and more severe a mother's depression, the greater the behavioral impairment in children.[37] As a result, PPD has been considered by Bright Futures, a leading pediatric health supervision guideline, as "one of the greatest risk factors for child behavioral and mental health problems".[38]

Treatment strategies for women with PPD have demonstrated varying effects on mothers and their children.[39,40] The US Preventive Services Task Force and clinical experts have endorsed antidepressant treatment and psychotherapies targeting mothers.[1,41,42] However, recent reviews show little evidence that effective treatment of maternal mood alone improves mother-infant interactions and results in improved child outcomes.[43,44] More intensive psychotherapeutic interventions that specifically target mothers and their interactions with their children have demonstrated improved infant development, emotional regulation, and attachment security.[45-53] However, these intensive interventions incur substantial costs and participant time commitments which limit their impact and scalability. Parenting programs aimed at improving a mother's parenting knowledge and skills have shown beneficial effects on mother-child relationships and child behaviors and development.[54-65] Unlike intensive psychotherapeutic interventions, they require a modest

commitment of time and energy on the part of new mothers and have been widely disseminated and scaled up across the US. However, the effects of parenting programs have received little study among women with PPD.[66-68]

1.1 Introduction

It isn't clear whether parenting programs tailored to women with PPD can improve mother-child interactions and ultimately child development and behavior. In previous studies, we and other investigators found that depressed women who attended group parenting programs reported improved parenting practices and decreased depressive symptoms.[66-68] A systematic review and meta-analysis of 48 clinical trials of parenting programs (not specifically targeting depressed parents) also found that group-based parenting programs were associated with significant short-term (<6 months) benefits on maternal mood and psychosocial well-being.[69] However, these few studies provide no information on the downstream effects of parenting programs targeting women with PPD on child development and behavior. In addition, given the potential short-term effects of parenting programs on maternal psychosocial well-being, it isn't clear whether sustained improvements in depressive symptoms are necessary to affect improvements in child development and behavior.

Observational studies of women with PPD and chronic depression help inform this application. They show that responsive and sensitive parenting mediates the effects of maternal depression on early child development, school readiness, and child behavior.[30,31,70] This suggests that responsive parenting can serve as a target engagement for studies of parenting interventions designed to improve child development among mothers with PPD. In addition, observational studies have shown that poverty and social support are important and likely moderate the association between PPD and child development.[70,71] Therefore, studies investigating parenting programs should investigate whether poverty and social support moderate effects on responsive parenting.

In a preliminary study that informs this proposal, we examined the effects of an adapted parenting program on parenting practices among mothers with depressive symptoms.[66,72] We adapted the Incredible Years (IY) Parents, Babies, and Toddlers program, an evidence-based parenting program, for use with depressed parents by the inclusion of depression psychoeducation.[73] We enrolled and randomized 61 mother-toddler dyads to immediate or delayed in-person group intervention. Those in the immediate intervention group received the adapted 12-week program and reported greater improvements in parenting disciplinary practices (Parenting Scale adjusted difference -0.4, 95% CI -0.7 to -0.1)) but similar changes in depressive symptoms (Beck Depression Inventory-II adjusted difference -3.4, 95% CI -8.7 to 1.9), social support (Multidimensional Scale of Social Support adjusted difference 0.3, 95% -0.4 to 0.9), and parenting stress (Parenting Stress Index Short Form adjusted difference -1.8, 95% CI -11.2 to 7.4) as women in the delayed intervention group. Although most (59%) women in the immediate intervention group attended at least one parenting session, few (10%) attended all 12 sessions with the mean number of sessions attended being 3.7 (range 0-12). Women reported multiple barriers to attendance including unstable housing, changing work schedules, and other children in the household to attend to. Our results suggest that a strategy utilizing parent training programs may improve the

parenting skills of depressed women and potentially improve child development, but adaptations are needed to improve participation among women with PPD.

1.2 Name and Description of Investigational Product or Intervention

Social Media-Based Parenting Program:

The parenting program consists of 8 weekly sessions using a Facebook platform with the following topics: depression psychoeducation and behavioral activation, infant temperament, play, feeding, safety, sleep, parent-child interactions, and shared book reading. Participants are enrolled in Facebook secret user groups, administered by a trained facilitator, in order to permit participants to view and comment on posted materials. Content and user identity are restricted to invited participants to maintain privacy. For each topic, we organize educational materials into video vignettes, narrated PowerPoint presentations, and written materials. The facilitator reviews and comments on postings daily, provides feedback to participants, and removes inappropriate postings if they occur. Facebook analytics for the secret groups are available to group administrators and will provide information on any sessions viewed (engagement) and counts of sessions viewed and comments posted (dosage).

MoodGym:

The Moodgym program is an evidence-based online cognitive behavioral treatment program that has been shown be effective at reducing depression symptoms in a meta-analysis of 11 trials (g=0.36, 95% CI 0.17-0.56). Moodgym contains five modules with interactive exercises, workbooks, anxiety and depression quizzes, and downloadable relaxation audio files that can be completed online without therapist interaction. We will supplement Moodgym with a facilitator contact by texting or email to check-in and encourage completion of intervention. *MoodGym will provide information on the number of sessions completed by participants (engagement and dosage).*

1.3 Relevant Literature and Data

We developed content for the program through a review of the literature on early infant parenting topics and incorporated depression psychoeducation and behavioral activation strategies to the program.[38,74-78] To validate content and format of the program, we convened two focus groups of women with PPD symptoms. Women were recruited using advertisements at participating practices and through direct referrals from clinicians. Focus groups lasted 1-2 hours and were conveniently held in the evenings at a participating practice. The focus groups were moderated by a trained facilitator using a previously piloted interview guide. Focus group participants were provided with an overview of the program, its format, and the topics derived from the literature review and were asked to submit comments and suggestions. Focus groups were audiotaped and transcribed. Based on focus group participant feedback, content for the program was revised and sessions reflecting the content were developed.

We developed a program of 8 weekly sessions for a Facebook format with the following topics depression psychoeducation and behavioral activation, infant temperament, play, feeding, safety, sleep, parent-child interactions, and reading. Women who screened positive (score >9) on the Edinburgh Postpartum Depression Scale (EPDS) at their child's two-month well child visit were recruited to participate in the program. We used Facebook secret user groups to convey the program content to participants.[79] A trained facilitator administered the Facebook secret user groups and permitted participants to view and comment on posted materials but restricted content and user identity only to invited participants to preserve privacy. For each topic we organized educational materials into video vignettes, narrated PowerPoint presentations, and written materials. Weekly content for each topic was released separately in three postings onto the Facebook site over the course of a week. The facilitator reviewed postings on a daily basis, commented on participants' postings, provided encouragement to participants, and removed inappropriate postings if they occurred.

We assessed feasibility through attendance and posting of comments on weekly Facebook groups. We assessed acceptability using a 5-point satisfaction scale at the conclusion of each weekly group. We recruited 18 eligible women from 3 urban practices in Philadelphia. Participants were predominantly African-American, single, with a high school education or less, or with a family income < $30,000. On average, 89% (range 78-100%) of participants attended weekly Facebook groups, and 69% (range 61-89%) of participants posted comments at weekly Facebook groups (Table 1). The mean overall satisfaction score was 4.5 (range 3-5).

We also examined preliminary outcomes of this Facebook parenting intervention on measures of parenting and depression. We conducted a small randomized controlled trial with 24 women with PPD symptoms. Participants were randomized to receive the parenting program through a social media or in-person group format. Twenty of the 24 (83%) women completed assessments pre- and post-intervention. We evaluated target engagement of the intervention, parenting competence, using the Parenting Sense of Competence Scale (PSOC), a validated self-report of parenting efficacy, and maternal depressive symptoms using the Beck Depression Inventory-II (BDI-II). Twenty-four mothers (mean age of 26 years; predominantly African American with limited economic resources) participated in the study. Linear regressions showed that the social media intervention resulted in significantly improved parenting competence (Effect Size 1.61) and decreased depression severity (Effect Size 0.96) compared to the in-person group (Table 2). Weekly attendance in the social media group was much greater (mean 83% vs. 3%) than in the in-person group. These results suggest that a parenting program adapted for a social media platform was feasible and acceptable among a low-income urban minority population and can improve parenting practices and reduce depressive symptoms. However, a more objective measure of target engagement as well as a link to signal improved child development is needed in future study

Table 2. Outcomes of Social Media-based Intervention

Measure	Social Media Group (N=12)	In Person Group (N=8)
BDI-II (SD)		
Baseline	29.5 (2.3)	23.4 (3.3)
Post	20.2 (2.2)	23.3 (4.9)
PSOC (SD)		
Baseline	67.8 (2.6)	78.3 (3.0)
Post	76.3 (3.4)	73.6 (3.7)

1.4 Compliance Statement

This study will be conducted in full accordance all applicable Children's Hospital of Philadelphia Research Policies and Procedures and all applicable Federal and state laws and regulations including 45 CFR 46 and the Good Clinical Practice: Consolidated Guideline approved by the International Conference on Harmonisation (ICH). All episodes of noncompliance will be documented.

The investigators will perform the study in accordance with this protocol, will obtain consent, and will report unanticipated problems involving risks to subjects or others in accordance with The Children's Hospital of Philadelphia IRB Policies and Procedures and all federal requirements. Collection, recording, and reporting of data will be accurate and will ensure the privacy, health, and welfare of research subjects during and after the study.

2 STUDY OBJECTIVES

The overall objective is to assess the effects of this theoretically-driven social media-based parenting program on responsive parenting and child development, the outcome of interest among mothers with PPD symptoms. We will assess target engagement, responsive parenting, of the program using an objective measure. Responsive parenting has been identified empirically as a significant mediator of child developmental outcomes in this population.[30,31,70]

2.1 Primary Objective (or Aim)

To determine whether the social media-based parenting program can improve responsive parenting among women with PPD symptoms, using the PCERA to measure the quality of affect and behavior in parent-child interactions.

2.2 Secondary Objectives (or Aim)

Secondary outcomes, including changes in EPDS, BDI-II, PSOC, and PSI-SF scores measured between baseline and the 3-month follow-up between groups, will be explored to determine if the effects of the parenting program are consistent with preliminary pilot findings. Descriptive statistics for demographic and poverty characteristics and PPD symptoms measured at baseline will be examined across the two treatment groups to assess the success of the randomization. . At the 3-month follow up, the intervention arm will be assessed with the TFI-8 to measure cohesion, and also be administered the Acceptability survey which measures feasibility of the parenting program. Additionally, at the 3-month mark, all participants will be administered the MoodGym Acceptability Survey to assess feasibility of the online depression treatment program.

3 INVESTIGATIONAL PLAN

3.1 General Schema of Study Design

To determine whether the social media-based parenting program can improve responsive parenting among women with PPD symptoms (Aim #1), we will conduct a prospective individually randomized group treatment trial. 75 eligible women who screen positive for

PPD at their infants' well child visit and their children will be consented, enrolled, and randomized as mother-child dyads 1:1 to receive a) the social media-based parenting program plus online depression treatment or b) online depression treatment alone. We chose a randomized design, because it is most effective in guarding against bias and will ensure that patients in both arms are similar in observed and unobserved characteristics. Treatment assignment will be done at the time of enrollment following informed consent and completion of the videotaped baseline PCERA. We will assess responsive parenting at baseline and 3 months post-enrollment. Cohesion will be measured for the intervention arm at 3 months post-enrollment.

3.1.1 Screening Phase

Families of eligible children will be recruited at the time of an office visit that results in a woman screening positive for PPD (EPDS score>9) at their infant's well child visit at a participating practice. Screening for PPD at an infant's well visit is standard of care at CHOP primary care practices. Recruitment will occur by telephone following an office visit using an electronic recruitment tool that permits clinicians to obtain permission for contact from families at an office visit. Electronic recruitment tools have become standard practice in PeRC and facilitate recruitment of patients across multiple studies. The electronic recruitment tool is an alert in EPIC that indicates that because the mother screened positive for PPD, she and her child may be eligible for a research study. If the mother provides permission to be contacted, her contact information will be sent securely through CHOP BusinessObjects to study staff. Potential subjects will be screened over the phone using the protocol inclusion and exclusion criteria. Caregivers of eligible children will be then scheduled for an in-person consent and will complete study visits at baseline, 1 month, 2 months, and 3 months (Table 1). While informed consent can take place at a separate visit and location from the baseline visit according to participant preference, the baseline visit will occur at a CHOP site (primary care office or other CHOP site) in order to facilitate adequate video recording. In the event that the baseline visit cannot be completed in-person, an alternative method of obtaining informed consent will be used. Following the telephone screen, caregivers of eligible children will be sent the informed consent document electronically through REDCap. The study team will then go over the document in detail with the eligible caregiver by phone. The e-consent function in REDCap will be used to obtain the caregiver's signature. The signed e-consent will then be stored within REDCap, and a copy of the form will be available to download and emailed securely to the caregiver. Additionally, baseline visit surveys may be administered online through REDCap and the PCERA video recording may be conducted remotely. If the PCERA is administered remotely, participants will be asked to videotape themselves free-playing with their child at home on a smart phone or tablet. They will then upload the video to a secure cloud-based service called BOX, that is available through a free mobile application and used by CHOP to securely store files. Instructions for recording home videos can be found in Appendix 14. Participants will also have the option of utilizing a secure video platform (e.g., Skype, BlueJeans, or other platform) where a study team member could record the mother and infant playing together. The recording would then be securely stored by the study team member. We will use all available means including letters, telephone calls, text messages, and emails to ensure data are collected thoroughly and systematically from all participants for follow-up measures. Participation incentives will include compensation to complete

study measures, and child birthday card mailings all of which have been used in our prior work (see approved studies 18-014807 and 15-012456) with urban populations to maintain >80% participant follow-up.[75]

3.1.2 Study Treatment Phase (start of the study intervention)

Women will complete measures of demographic characteristics, family income, social support (MSPSS), depressive symptoms (EPDS, BDI-II), parenting competence (PSOC), and parenting stress (PSI-SF) at baseline. Parent-child dyads will be videotaped before initiation of the parenting program using the Parent-Child Early Relational Assessment (PCERA). Women in both study arms will be enrolled in MoodGym, an evidence-based online Cognitive Behavioral Therapy (CBT) program for depression. Women randomized to the parenting program will be invited to enroll in a Facebook secret user group and participate in the 8-week online parenting program. Women will complete monthly assessments of PPD depressive symptoms using the EPDS and mental health services use using a question from the National Comorbidity Study (NCS). At 3 months post-enrollment, women will complete measures of parenting competence and parenting stress, depressive symptoms, parent-child dyads will complete the PCERA, the Moodgym Acceptability Survey, and women in the intervention arm will complete the Therapeutics Factor Inventory-8 (TFI-8) and the Acceptability Survey. If Study Visits 1 and/or 4 cannot be completed in-person, surveys may be administered online through REDCap and the PCERA may be conducted remotely. If the PCERA is administered remotely, participants will be asked to videotape themselves free-playing with their child at home on a smart phone or tablet. They will then upload the video to a secure cloud-based service called BOX,that is available through a free mobile application and used by CHOP to securely store files. Instructions for recording home videos can be found in Appendix 14. Participants will also have the option of utilizing a secure video platform (e.g., Skype, BlueJeans, or other platform) where a study team member could record the mother and infant playing together. The recording would then be securely stored by the study team member. To assess feasibility, the Acceptability Survey will be administered to participants in the parenting program to assess their perceptions of the parenting program, the extent to which it meets their needs, and barriers that impeded their participation in the program. Using intention-to-treat analysis, we will determine differences in change scores in responsive parenting (PCERA parenting subscales) between groups as the main outcome. We will also examine differences in parenting stress, parenting competence, and depressive symptoms as secondary outcomes. As a secondary analysis, we will examine effects of dosage (duration of participation and number of sessions completed) on PCERA parenting subscales and secondary outcome measures among those in the parenting group. To analyze the Acceptability Survey, we will examine mean acceptability scores for each PWD session for participants in the intervention arm, and mean acceptability scores for the MoodGym session for all participants through the MoodGym Acceptability Survey. We will also qualitatively analyze the open-ended questions to help inform the acceptability scores.

3.2 Allocation to Treatment Groups and Blinding

Women will be recruited at the time of a well child visit for their < 8 months old infant using an electronic recruitment alert and will undergo written informed, either in-person or electronically, consent at their first study visit. Following informed consent and completion

of the videotaped baseline PCERA, women will be randomized 1:1 to either the parenting program plus online CBT or online CBT alone. Randomization will be accomplished in advance by the study biostatistician using computer-generated random numbers. The initial randomization will be stratified by practice site to ensure balance at the practice level between groups. Allocation concealment (blinding of the treatment assignment) will be implemented using sealed, opaque envelopes, along with stratification, and randomly permuted blocks of unequal sizes (to prevent providers and patients from manipulating the randomization).

3.3 Study Duration, Enrollment and Number of Sites

3.3.1 Duration of Study Participation

The study duration per subject will be approximately 3-6 months.

3.3.2 Total Number of Study Sites/Total Number of Subjects Projected

The study will be conducted at approximately 6 CHOP primary care practices, starting with 3-4 sites.

Recruitment will stop when approximately 75 mother-child dyads are enrolled. It is expected that approximately 75 dyads will be enrolled to produce 60 evaluable dyads.

3.4 Study Population

3.4.1 Inclusion Criteria

Women who:

1) Are >18 years old
2) Screen positive for postpartum depression (score>9) on the EPDS at a participating pediatric practice
3) Have an infant <8 months of age
4) Speak and Read English
5) Have Access to a smart phone or computer tablet with internet access
6) Have completed an informed consent

Children who:

7) Are < 8 months old

3.4.2 Exclusion Criteria

Women who:

1) Report suicidality (i.e., suicidal ideation and/or behavior) on the EPDS (Question #10) at enrollment.

2) Report severe depressive symptoms (EPDS>20) at enrollment.

3) Have a substantiated report of child maltreatment

Children who:

1) Were born premature (estimated gestational age<35 weeks)

2) Have been diagnosed with congenital malformations or genetic syndromes which place them at risk of developmental delays

3) Are already currently receiving early intervention services for developmental delays at baseline

Subjects that do not meet all of the enrollment criteria may not be enrolled. Any violations of these criteria must be reported in accordance with IRB Policies and Procedures.

4 STUDY PROCEDURES

4.1 Screening Visit

List the timing and all of the procedures to be performed at the screening visit. This can be a simple bullet list.

- Informed Consent
- Medical Record Review
- Review of Inclusion/Exclusion Criteria
- Randomization

4.2 Study Treatment Phase

Over the course of each subject's participation, the subject will have a baseline study visit and 3 monthly follow-up visits. After being screened at baseline, participants will complete demographics, BDI-II, PSI-SF, PSOC, PCERA, MSPSS, and poverty measures. At each of the three follow-up visits, measures of depression (EDPS) and an NCS item will be completed. At the final follow up, three months after enrollment, participants will complete the PSI, PSOC and PCERA measures again, the MoodGym Acceptability Survey and participants in the intervention arm will complete the TFI-8 and the Acceptability Survey.

4.2.1 Visit 1 (Baseline)

- Demographics Measure
- EPDS
- BDI-II

- PSI-SF
- PSOC
- PCERA
- MSPSS
- Poverty
- Review of child's medical record

4.2.2 Visit 2 (1-month follow up)

- EPDS
- NCS Item

4.2.3 Visit 3 (2-month follow-up)

- EPDS
- NCS Item

4.2.4 Visit 4 (3-month follow-up)

- EPDS
- BDI-II
- NCS Item
- PSI-SF
- PSOC
- PCERA
- MoodGym Acceptability Survey
- TFI-8 (Intervention arm only)
- Acceptability Survey (Intervention arm only)

4.3 Unscheduled Visits

Unscheduled visits are not anticipated.

4.4 Subject Completion/Withdrawal

Subjects may withdraw from the study at any time without prejudice to their care. They may also be discontinued from the study at the discretion of the Investigator for lack of adherence to the study visit schedule or any AEs. The Investigator may also withdraw subjects who violate the study plan, or to protect the subject for reasons of safety or for administrative reasons. Additionally, if a subject is enrolled but does not complete the videotaped baseline PCERA before the start of the intervention, regardless of the group they were randomized to, they will be withdrawn from the study. It will be documented whether or not each subject completes the study. If the Investigator becomes aware of any serious, related adverse events after the subject completes or withdraws from the study, they will be recorded in the source documents and on the CRF.

4.4.1 Early Termination Study Visit

Subjects who withdraw from the study following screening may receive recommendations for follow up per their specific needs.

5 STUDY EVALUATIONS AND MEASUREMENTS

5.1 Screening and Monitoring Evaluations and Measurements

5.1.1 Medical Record Review of Child

Include a listing of the variables that will be abstracted from the medical chart (paper or electronic).

- Date of birth
- Gestational age
- Sex
- Problem list
- Chart review for developmental assessments, depression screenings, child maltreatment
- Contact information
- Age of mother
- Languages spoken/read

5.1.2 Other Evaluations, Measures

Measures proposed for this phase of the study correspond to our experimental therapeutics framework and will assess differences in responsive parenting as the measure of target engagement. This is consistent with observational studies which have shown that responsive parenting mediates the effects of maternal depression on early child development and can

serve as a target for intervention engagement.[30,31,70] Following written informed consent, women will complete a baseline visit. Measures of demographic and biological variables (age, sex, race/ethnicity, maternal education level, and family structure), social support, and poverty (family income level) will be collected by research staff at baseline to assess success of randomization. Depressive symptoms and outside mental health treatment will be measured monthly using the EPDS and an item from the National Comorbidity Survey (NCS) concerning any service use.[96] Depressive symptoms will also be measured at baseline and at the 3-month follow up using the BDI-II. Women who report EPDS scores >20, BDI-II scores 29-63, or who report suicidality (EPDS question #10, BDI-II question #9) will remain in the study and will be contacted immediately and provided with assistance in obtaining urgent mental health referrals. The research team will also contact women with severe depression (EPDS scores>20, BDI-II scores 29-63) or suicidality weekly to monitor their symptoms and treatment. Social support will be measured at baseline by the Multi-dimensional Scale of Perceived Social Support (MSPSS), a 12-item scale that assesses perceived social support from family, friends, and a significant other.[97] Parenting will be measured at baseline and at follow-up 3 months later using 3 separate instruments: The Parenting Sense of Competence Scale (PSOC), the Parenting Stress Index-Short Form (PSI-SF), and the Parent-Child Early Relational Assessment (PCERA). At the 3-month follow up, cohesion will be measured with the TFI-8 and feasibility of the parenting program with be measured with the Acceptability Survey Additionally, feasibility of the online depression treatment program, MoodGym, will be measured at the 3-month follow up using the MoodGym Acceptability Survey. In the event that the baseline and/or 3-month follow up visits cannot be completed in person, study procedures may be conducted virtually. Surveys administered at baseline and at the 3-month follow up (see Table 1) may be administered online through REDCap. The PCERA may be conducted remotely as well. If the PCERA is administered remotely, participants will first be contacted by phone or email and asked to videotape themselves free-playing with their child at home on a smart phone or tablet. They will then upload the video to a secure cloud-based service called BOX, that is available through a free mobile application. BOX is used widely by CHOP as an institution to securely store files. Participants will also have the option of utilizing a secure video platform (e.g., Skype, BlueJeans, or other platform) where a study team member could record the mother and infant playing together. The recording would then be securely stored by the study team member. Once uploaded, videos will be labeled with each participant's corresponding identification number, to further protect their identifiable information. Only the study team will have access to these video files. Instructions detailing the process of recording and uploading the home videos will be emailed to each participant prior to completing the recordings.

The PSOC is a validated 17-item self-report measure of parenting self-esteem and competence and consists of two factors: satisfaction and efficacy.[98] The PSI-SF consists of 36 items that measure parenting stress.[99,100] The PCERA is a validated 65-item (29 parental, 28 child, and 8 dyadic items) videotape assessment designed to measure the quality of affect and behavior in parent-child interactions and will serve as the primary measure of responsive parenting.[101,102] The PCERA uses ratings that are based on observations of 5-minute videotaped interactions with parent-infant dyads engaged in free play and is designed to measure therapeutic change and its effects on the parent-child interaction. The PCERA

has been shown to possess good interrater reliability, internal consistency, discriminant and concurrent validity, and sensitivity to change.[51,102-104] The PCERA contains 8 subscales (3 parental, 3 child, 2 dyadic) of which we postulate that a parenting program will have a positive impact on three responsive parenting subscales: 1) Parental Positive Affective Involvement and Verbalization, 2) Parental Negative Affect and Behavior, and 3) Parental Intrusiveness, Insensitivity, and Inconsistency. At the follow-up visit, we will also conduct brief audiotaped semi-structured interviews with participants in the parenting program to assess their perceptions of the parenting program, the extent to which it meets their parenting needs, and barriers that impede their participation in the social media-based program. This information can be used to revise the parenting program, particularly if target engagement is not met. An interview guide will be developed during this phase of the study.

Edinburgh Postnatal Depression Scale (EPDS): Secondary, Baseline, 1 month, 2 months, 3 months.

The EPDS is a validated 10-item self-report measure of depressive symptoms with strong evidence for reliability, validity, and utility in varying populations. It has been used extensively in mental health research and provides cutpoints to determine the severity of depressive symptoms. It includes a question on suicidal thoughts and wishes (#10) that will be used to monitor for suicidality. The total score will be used with scores of 10 or higher representing minor or moderate depression and scores of 20 or greater representing severe depression.

Beck Depression Inventory (BDI-II): Secondary, Baseline & 3 months.
The BDI-II is a 21-item self-report tool that measures the severity of depression and includes two subscales: cognitive and somatic. It has been well validated, and widely used, with scores 14-19 indicating mild depression, 20-28 moderate depression, and 29-63 severe depression. The total score will be used.

Parenting Sense of Competence Scale (PSOC): Secondary, Baseline & 3 months.
The PSOC is a validated 17-item self-report measure of parenting self-esteem and competence and consists of two factors: satisfaction and efficacy. Response categories are on a 6-point likert-scale from strongly disagree to strongly agree. The total score (which includes the sum of the two factors) will be used.

Parenting Stress Index-Short Form (PSI-SF): Secondary, Baseline & 3 months.
The PSI-SF is a validated 36-item scale that measures parenting stress. It has been shown to have excellent internal consistency and to be positively associated with maternal psychological distress. Scores on the PSI-SF correlate well with the full PSI. The total score will be used.

Patient Child Early Relational Assessment (PCERA): Primary, Baseline & 3 months.
The PCERA is a validated 65-item (29 parental, 28 child, and 8 dyadic items) videotape assessment designed to measure the quality of affect and behavior in parent-child interactions and will serve as the primary outcome measure. The PCERA uses ratings that are based on observations of 5-minute videotaped interactions with parent-infant dyads

engaged in free play at a research lab at CHOP or offsite at an appropriate location. The PCERA has been shown to possess good interrater reliability, internal consistency, discriminant and concurrent validity, and sensitivity to change. The PCERA contains 8 subscales of which 3 parenting subscales will be the focus: 1) Parental Positive Affective Involvement and Verbalization, 2) Parental Negative Affect and Behavior, and 3) Parental Intrusiveness, Insensitivity, and Inconsistency. Mothers are instructed to play with their infant as they normally would using a set of age-appropriate toys provided for their use in the free play. Administration and coding will follow the PCERA manual.

National Comorbidity Survey (NCS): Secondary, Baseline, 1 month, 2 months, 3 months.
We will include a question from the NCS on prior mental health services use in the past month: "In the past month, did you receive treatment for problems with your emotions or nerves, or your use of alcohol or drugs?" We will consider mental health service use to have occurred in the past month if a mother responds affirmatively to this question. Additionally, if a mother responds affirmatively to the initial NCS item, a follow-up question will be asked to determine the specific types of services that were accessed: "If yes, what type of treatment did you receive?"

Multi-dimensional Scale of Perceived Social Support (MSPSS): Secondary, Baseline.
The MSPSS is a 12-item scale that assesses perceived social support from family, friends, and a significant other. Response categories are on a 7-point likert-scale from very strongly disagree to very strongly agree. The total score will be used.

MoodGym Acceptability Survey: 3 months.
The Acceptability survey is a 1-item scale with 2 additional open ended questions that will be used to assess feasibility of the online depression treatment program, MoodGym. The total score will be used and the open ended questions will be qualitatively analyzed to help inform the acceptability scores.

Therapeutic Factors Inventory-8: 3 months, Intervention arm only
The TFI-8 is a validated 8-item scale that is used to measure cohesion and is continuous process monitoring for therapy groups. Scores on the TFI-8 correlate well with the full TFI. The total score will be used.

Acceptability Survey: 3 months, Intervention arm only
The Acceptability survey is a 10-item scaled with 3 additional open ended questions that will be used to assess feasibility of the parenting program. The total score will be used and the open ended questions will be qualitatively analyzed to help inform the acceptability scores.

5.2 Safety Evaluation

Subject safety will be monitored by adverse events reporting. As this study is not greater than minimal risk serious adverse events are not anticipated

6 STATISTICAL CONSIDERATIONS

6.1 Primary Endpoint

The primary endpoint will be the change in responsive parenting (PCERA) between baseline and visit 4.

6.2 Secondary Endpoints

Secondary outcomes, including changes in EPDS, BDI-II, PSOC, and PSI-SF scores measured between baseline and the 3-month follow-up between groups, will be explored to determine if the effects of the parenting program are consistent with preliminary pilot findings. Mean scores on the Acceptability Survey and MoodGym acceptability Survey will be used to assess feasibility of the parenting program as well as the online depression treatment program.

6.3 Statistical Methods

6.3.1 Baseline Data

Descriptive statistics for demographic, behavioral, and environmental characteristics measured at baseline will be examined across the two treatment groups to assess the success of the randomization.

6.3.2 Efficacy Analysis

The primary analysis will be based on an intention to treat approach and will include all subjects randomized at Visit 1.

The primary efficacy endpoint will be the change in PCERA between Visit 1 and Visit 4.

Secondary endpoints will include the changes in EPDS, BDI-II, PSOC, and PSI-SF scores measured between baseline and the 3-month follow-up between groups, will be explored to determine if the effects of the parenting program are consistent with preliminary pilot findings. Mean scores on the Acceptability Survey and MoodGym acceptability Survey will be used to assess feasibility of the parenting program as well as the online depression treatment program.

6.4 Sample Size and Power

Our target sample size accounting for clustering by practice site for dyads with complete 3-month follow-up data is 60 mother-child dyads. Assuming at least 80% follow-up, the number needed to recruit this final sample size is 75 (30% of potentially eligible women across all 4 urban pediatric practices in 2016). Since a partial goal of the proposed intervention is to increase patient engagement in the parenting program, the rate of drop out is likely to be lower among the intervention group. If we conservatively assume that the attrition rate among control participants is triple (30% vs. 10%) that of intervention patients, the sample of patients with complete follow-up will consist of approximately 26 control dyads and 34 intervention dyads (Figure 2). Using changes in the PCERA parenting subscale scores as the primary outcome, we assert that the proposed parenting intervention would be successful if it results in an effect size (ES) ≥0.8 on one or more of the 3 subscales

between intervention groups. This is similar to the difference in subscale scores observed between groups in a novel mother-infant therapy group trial and is half the difference (ES=1.6) we observed in PSOC scores in our preliminary study.[51] Thus, based on the proposed sample size, we would obtain 80% power to detect an effect size between 0.79-0.96 between groups assuming an interclass correlation coefficient (ICC) between 0.01 to 0.1 among participating practices. Our target sample size of 34 mother-child dyads who complete the parenting intervention is sufficient for the qualitative interviews to obtain saturation of themes.

7 SAFETY MANAGEMENT

7.1 Clinical Adverse Events

Clinical adverse events (AEs) will be monitored throughout the study.

7.2 Adverse Event Reporting

Since the study procedures are not greater than minimal risk, SAEs are not expected. If any unanticipated problems related to the research involving risks to subjects or others happen during the course of this study (including SAEs) they will be reported to the IRB in accordance with CHOP IRB SOP 408: Unanticipated Problems Involving Risks to Subjects. AEs that are not serious but that are notable and could involve risks to subjects will be summarized in narrative or other format and submitted to the IRB at the time of continuing review.

8 STUDY ADMINISTRATION

8.1 Treatment Assignment Methods

8.1.1 Randomization

75 eligible women will be consented, enrolled, and randomized 1:1 to receive the a) 8-week social media-based parenting program plus MoodGym or b) MoodGym alone. Women will complete measures of demographic characteristics, family income, social support, depressive symptoms, parenting competence, and parenting stress at baseline. Parent-child dyads will be videotaped before initiation of the parenting program using the Parent-Child Early Relational Assessment (PCERA). Women in both study arms will be enrolled in MoodGym, an evidence-based online CBT program for depression. Women randomized to the parenting program will be invited to enroll in a Facebook secret user group and participate in the 8-week online parenting program. Women will complete monthly assessments of PPD depressive symptoms using the EPDS and mental health services use using a question from the NCS. At the 3-month visit, all participants will complete the MoodGym Acceptability Survey. Women in the social media-based parenting program intervention will complete the TFI-8 and the Acceptability Survey at the 3 month visit.

8.1.2 Blinding

Allocation concealment (blinding of the treatment assignment) will be implemented using sealed, opaque envelopes, along with stratification, and randomly permuted blocks of unequal sizes (to prevent providers and patients from manipulating the randomization).

8.2 Data Collection and Management

All records generated during this study will be kept confidential in accordance with Institutional policies and HIPAA on subject privacy. The Investigator and other site personnel will not use such data and records for any purpose other than conducting the study.

To ensure confidentiality of information, data will be stripped of potential identifiers, and all written and computerized files will be indexed by a unique identification number. Only research staff will have access to this information and to a separate master list. All data for these study procedures will be maintained on CHOP's secure research server, and all analyses will be performed on de-identified data only. All collected study measures will be entered directly into a REDCap database maintained and protected on this secure research server. The unique identifiers will be used to track enrolled families over the course of the study. Confidentiality will also be maintained by use of subject code numbers in all presentations and publications. Each member of the research team, including investigators, research assistants, and stakeholder-investigators will receive appropriate training in human subjects research and patient confidentiality.

Unique identifiers will be created for each subject in the study. REDCap will be used to store the data. A master list containing PHI and subject ID number will be kept separate from data forms (electronic and paper). The master list will be kept using password-protected files. These files will be encrypted and maintained on the CHOP secure server to ensure security. Participants' information will be stored in the REDCap database and configured to export data without PHI. All de-identified records will be retained forever. De-identified data will be shared with the study sponsor. Stored data and patient identifiers will be kept for 6 years subsequent to the study completion, and possibly longer if required by the sponsor.

8.3 Confidentiality

All data and records generated during this study will be kept confidential and in accordance with institutional policies and HIPAA on subject privacy. Participation in all aspects of the proposed study is completely voluntary. The research team will institute strict procedures to maintain confidentiality. Subjects will be assigned a unique identification code that will be used as the sole identifier. The data will only be shared with the investigative team during the implementation of the study and results will only be presented in aggregate form. Any results obtained cannot be related to the original source, so no results would be provided to the patient, healthcare provider, or insurance provider. All study information will be maintained on a secure password-protected server with regular backup. Per standard NIH guidelines, a Certificate of Confidentiality (CoC) will be automatically generated for this NIH-funded study.

Every 6 months, the study sponsor NIMH requires a data transfer to the NIMH Data Archive (NDA). During the course of the study and after its completion, the research team will send de-identified data to the NDA repository where it will be stored and managed. Additionally, any necessary study data will be transmitted accordingly to Clinicaltrials.gov.

8.4 Regulatory and Ethical Considerations

8.4.1 Data and Safety Monitoring Plan

The investigative team will implement a data and safety monitoring plan to ensure the safety of study participants and their families and to ensure the integrity of the data collected. Research staff will provide reports of preliminary data and adverse events to the project Data and Safety Monitoring Board (DSMB) and on an annual basis throughout the duration of the study. The DSMB will be overseen by clinical investigators TBN from the CHOP Research Institute who are not investigators on the study.

The DSMB will meet annually to review data integrity and patient safety, particularly with regards to reports of child maltreatment. The DSMB will make determinations regarding additional procedures to implement to protect the safety of study participants and to ensure integrity of data. The DSMB will also review current study procedures with regards to participant recruitment, retention, intervention procedures, and study measures and make recommendations to reduce participant burden and ensure the timely and efficient completion of study milestones. In the unlikely event of an adverse outcome associated with this study protocol, e.g. disclosure of patient information, it will be documented and discussed with the research team, and reported to the CHOP IRB and the NIMH, if appropriate, on an annual basis. Any serious adverse events, e.g. substantiated reports of child maltreatment or suicidality, will be reported to the CHOP IRB, the DSMB, and to NIMH within one business day of discovery (telephone, fax, email, eIRB) with a full report submitted in eIRB within 48 hours of the initial notification. In addition, appropriate agencies, e.g. Child Protective Services, will be promptly notified of any serious adverse events to comply with mandated reporting requirements.

8.4.2 Risk Assessment

The research involves the collection of sensitive and protected health information from participants. The risk of participation is considered minimal. There is a potential risk of breach of confidentiality of information and study results about individuals. This risk is minimized by measures taken by the study team to ensure confidentiality: use of secure files, storing data on secure computers, using unique study identifiers, de-identification of data prior to analysis, and obtaining a Certificate of Confidentiality through NIH. A second risk is that participants may become uncomfortable in completing study measures. If this occurs, the protocol will allow participants to stop at any time. Should any specific concerns arise throughout the project period, the CHOP IRB will be promptly informed. Since the purpose of the intervention is to help women improve their parenting skills, we expect that adverse consequences due to the intervention will be extremely rare and unlikely. However, we recognize that there is a risk of suicidality, worsening depression, and child maltreatment among this population, so we will monitor for suicidality, worsening depression, and child maltreatment at all study visits, contacts, and intervention procedures with participants.

Should suicidality or worsening depression be identified, we will implement a suicide prevention and depression treatment plan to assess immediate risk for harm and secure treatment. Should child maltreatment be suspected, we will implement a child abuse reporting plan to comply with all mandated reporting laws.

8.4.3 Potential Benefits of Trial Participation

Participating mothers may benefit directly from inclusion in this study if their depressive symptoms and parenting are improved as a result of the parenting intervention. In addition, participating infants may benefit directly from the study if their interactions with their mothers are improved as a result of the intervention. However, these benefits cannot be guaranteed. This parenting intervention may be replicated and scaled up in different care settings and thus generate generalizable knowledge. Further, the information obtained will be disseminated as widely as possible, including publication in peer-reviewed journals and policy briefs and presentations at scientific and lay conferences.

8.4.4 Risk-Benefit Assessment

Given the minimal risk nature of the study, the risks are considered reasonable in relation to the potential benefit to be gained.

8.5 Recruitment Strategy

Potentially eligible urban pediatric practices affiliated with CHOP have all implemented PPD screening using the Edinburgh Postnatal Depression Scale at 1-, 2-, and 4-month well child visits. Eligible women who screen positive for PPD at their infant's well child visit at a participating practice will be asked for permission for contact at the time of an office visit using an electronic recruitment tool. This tool permits clinicians to obtain permission for contact from eligible women at an office visit and to refer eligible patients to research staff. Electronic recruitment tools have become standard practice at CHOP and facilitate recruitment of patients across multiple studies. The electronic recruitment tool is an alert in EPIC that indicates that because the mother screened positive for PPD, she and her child may be eligible for a research study. If the mother provides permission to be contacted, her contact information will be sent securely through CHOP BusinessObjects to study staff. Those who consent for contact will be recruited by telephone by research staff who will explain the aims of the study, the nature of participation, risks and benefits of the study, and the voluntary nature of participation. Families who express interest based on this recruitment phone call will then be scheduled for an in-person meeting to complete written informed consent at their participating practice or a location of their choice before enrolling in the study. In the event that the baseline visit cannot be completed in-person, an alternative method of obtaining informed consent will be used. Following the telephone screen, caregivers of eligible children will be sent the informed consent document electronically through REDCap. The study team will then go over the document in detail with the eligible caregiver by phone. The e-consent function in REDCap will be used to obtain the caregiver's signature. The signed e-consent will then be stored within REDCap, and a copy of the form will be available to download and emailed securely to the caregiver. Participants will only be randomized to treatment arms following informed consent. We will maintain enrollment data on the number of potentially eligible women who present at each practice, the proportion who consent for contact, and the proportion who enroll in the study in order to ascertain whether our recruitment strategy is successful.

Among eligible urban practices in 2016, there were 250 women who screened positive for PPD. We would need to recruit 75 (30%) eligible mother-child dyads in phase 1 and 75

(30%) eligible mother-child dyads in phase 2 of the study. This translates into 1-2 participants being enrolled per week, which is similar to the number we successfully recruited into our preliminary pilot trial using the above recruitment strategy. We will monitor recruitment weekly by reviewing the proportion of eligible participants who consent for contact among those who screen positive for PPD at office visits and the proportion of participants who enroll in the study among those who consent for contact. We will also monitor the race/ethnicity of enrollees to ensure that we are achieving a sample representative of the participating practices (see enrollment tables). Should enrollment lag, we will consider expanding recruitment from 3-4 practices to all 6 urban pediatric practices affiliated with CHOP. We will also consider implementing in-person recruitment at offices should consent for contact lag.

8.6 Informed Consent/Assent and HIPAA Authorization

Following the screening via review of the medical record, eligibility for study participation will be explained via phone. During the research staff visit subsequent to the screening process, written informed consent will be completed. Research staff will discuss the study aims, procedures, risks and benefits, alternatives to participation, and confidentiality protocols with the parent. Research staff will speak to the parent about the voluntary nature of participation and provide the potential subject with the opportunity to ask questions about the study and its risks and benefits. Families who express interest based on this recruitment phone call will then be scheduled for an in-person meeting to complete two copies of the informed consent form: one will be kept for study purposes and the other will be provided to the consenting parent. In the event that the baseline visit cannot be completed in-person, an alternative method of obtaining informed consent will be used. Following the telephone screen, caregivers of eligible children will be sent the informed consent document electronically through REDCap. The study team will then go over the document in detail with the eligible caregiver by phone. The e-consent function in REDCap will be used to obtain the caregiver's signature. The signed e-consent will then be stored within REDCap, and a copy of the form will be available to download and emailed securely to the caregiver. In order to give parental permission for the child to participate, the consenting mother must be at least 18 years old. Parents will be provided with plenty of time to ask questions and to decide whether they want to participate. Parents will be explicitly instructed that they are free to choose to participate and that their decision to participate will not affect the health care they or their children receive at participating practices.

8.7 Payment to Subjects/Families

8.7.1 Reimbursement for travel and parking

Transportation with Lyft will be arranged for participants who have a car seat for Study Visits 1 and 4 through CHOP's Family and Visitor services. In the event that the participant does not have a car seat, the participant will be reimbursed on their Clincard for their roundtrip travel based on mileage.

8.7.2 Compensation for cellular data charges

Participants will be compensated $50 a month for 3 months of cellular data charges.

8.7.3 Payments to parent for time and inconvenience (i.e. compensation)

Participants will be compensated $50 for completion of their baseline surveys, $5 a month for completion of three months for the monthly surveys, and $50 for completion of their 3-month surveys. All payments will be made in the form of pre-paid, CHOP-issued debit cards. Additionally, if participants choose to arrange their own transportation to study visits, the study team will provide a courtesy parking pass that will be given to them at the time of the visit.

8.7.4 Gifts

No other gifts will be given.

9 PUBLICATION

This study will be registered with ClinicalTrials.gov following IRB approval of the final protocol and before any potential patients and their families are enrolled in the study. All study data will then be reported to the ClinicalTrials.gov site. Additionally, all arising publications of Study data and analyses will follow the set of guidelines outlined in the CHOP publications policy manual.

The research team plans to work closely with key stakeholders to disseminate and implement the findings of the research study into accessible and usable formats in research, clinical, and community-based settings. We will target findings to state and national policymakers, county EI agencies across the state, parent advocacy groups, and pediatric practices using social media, policy briefs, mass emails, and newsletters. We will work with PolicyLab at CHOP to develop dissemination plans. PolicyLab has extensive experience distilling research findings into policy-relevant summaries and disseminating research findings to end-users. We will also utilize traditional approaches such as peer-reviewed publications and presentations at national meetings to disseminate findings to other researchers.

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APPENDIX

See attached.