**Pragmatic Effectiveness / Implementation Trial of Mobile-First Web-Based Mindfulness Based Cognitive Therapy for Prevention of Perinatal Depression**

**SPECIFIC AIMS**

An increasing number of digital mental health technologies such as web-based programs and mobile apps are being developed to expand access to mental health treatments delivered in a cost-effective manner. Although efficacy trials of these technologies have often demonstrated improved patient outcomes, especially when used in combination with supportive coaching, (Mohr, 2017, Clarke et al, etc.) more widespread implementation and evidence of their effectiveness in routine care settings is lacking. Developing digital mental health technologies that are scalable and effective in real world clinical settings is therefore a priority for mental health services research.

One area of significant public health concern in which developing and testing implementation of digital mental health technology may be of particular benefit is for the treatment for perinatal depression. Approximately 30-40% of women with histories of depression experience relapse during the perinatal period, a majority show poor adherence to the most common prevention treatment, antidepressant medication, and a majority express a preference for non-pharmacologic prevention interventions. (Goodman et al, 2013; Dimidjian and Goodman, 2014) However, effective and easily accessible non-pharmacologic interventions are not widely available. Inadequate preventive treatment for depression may increase risk for both mother (depressive relapse and problems providing the sensitive, responsive care that infants need), and infants (preterm birth, low birthweight, and problems attaining developmental norms when relapse occurs). In addition, the cost to healthcare systems and society of untreated perinatal depression for women and their offspring can be substantial. It is therefore imperative to test the implementation of effective, non-pharmacological, and scalable treatments to reduce the risk of depression relapse in the perinatal period.

Mindfulness Based Cognitive Therapy (MBCT) is one of the most promising preventive interventions for adults, including pregnant women, with recurrent depression, demonstrating significant reductions in rates of depressive relapse and residual depressive symptoms. MBCT is an eight-session behavioral group intervention that specifically targets risk factors for depressive relapse through a combination of mindfulness meditation and movement, psychoeducation, and cognitive-behavioral strategies. However, in-person MBCT groups are difficult to scale up by health systems, and they may pose logistic challenges for participating pregnant women, many of whom must arrange child care and transportation to clinics, thus limiting access to and uptake of the intervention. Because of these limitations, our research team developed and refined a web-based version of MBCT with content specifically tailored to pregnant women at risk for recurrent depression. Called Mindful Mood Balance (MMB) for Moms, it is a mobile-first web-based program (allowing access via phone, tablet or computer) that includes the eight MBCT modules and features multi-modal content (text, video, audio, downloadable homework templates) delivered by experts, and designed to enhance user engagement. Beta testing of the program at Kaiser Permanente Colorado (KPCO) was conducted by the research team and usability assessment was completed by obstetricians, other clinicians and patient consultants with lived experience of perinatal depression, yielding a low cost, potentially scalable version of MBCT that may increase access to an effective non-pharmacologic treatment for preventing perinatal depression.

The critical next phase of our work is to evaluate potential of MMB for Moms to be more widely adopted, implemented and sustained as an effective intervention across heterogeneous patient populations and health care systems. In response to RFA-MH-XX, Announcement for A Practice-Based Research Network to Transform Mental Health Care: Science, Service Delivery & Sustainability, we propose a large pragmatic hybrid type II, multisite randomized effectiveness--implementation trial (Curran et al, 2013, 2018) comparing MMB for Moms to usual care (UC) among pregnant women at risk for recurrent depression. The topic of this proposed trial is of high value to the participating healthcare systems concerned about improving the quality of care for perinatal mood disorders, and it directly aligns with the NIMH priorities in perinatal mental health to 1) conduct studies of effective and innovative non-pharmacological alternatives to one-on-one interventions to identify, prevent, and treat perinatal mental disorder, including preventing postpartum relapse; and 2) leverage technology to improve access to care and mental health and functional outcomes. In addition, we will use strategies developed from implementation science to maximize the likelihood of successful adoption and scale up efforts.

**The proposed pragmatic trial will address several important questions to determine the scalability, effectiveness, and incremental cost effectiveness of MMB for Moms**: First, can MMB for Moms be adapted to, scaled up, and sustained across multiple practice settings representing diverse patient populations and heterogeneous groups of health care providers? Second, is MMB for Moms effective for preventing depressive relapse and secondarily for improving infant outcomes and maternal functioning when more widely implemented in a web-based format? Third, what is the incremental cost effectiveness of MMB for Moms relative to UC, and, as a key factor in its sustainability, if the program is effective, are health systems willing to pay for the sustainability of MMB for Moms?

Led by a well-established multi-disciplinary team of investigators within the Mental Health Research Network (MHRN) and leveraging multiple efficiencies from our prior successful collaborations, the proposed pragmatic trial will address these questions by randomly assigning ### pregnant women at risk for recurrent depression across ### healthcare systems to (1) 8 mobile-first web-based sessions of MMB for Moms plus usual care augmented with digital and phone-based coaching support, or (2) UC, consisting of routine screening for depression and referral to behavioral health services.

We will use the Accelerated Creation-to-Sustainment (ACTS) model to guide our efforts for the implementation trial. (Mohr, 2017) The ACTS model includes 2 basic iterative functions (design and evaluate) across 3 general phases of an implementation trial (Create, Trial, and Sustain). We will focus on the Trial phase that requires evaluation of both effectiveness and implementation of MMB for Moms. Consistent with an implementation trial, investigators at each site will engage obstetrics, behavioral health, and healthcare administrator stakeholders, as well as patients with lived experience of perinatal depression, to serve as research collaborators in the efforts to adopt, implement, and sustain MMB for Moms within their respective healthcare systems. These stakeholders will assist with strategies for adapting MMB for Moms to their respective sites and identify site-specific factors that may facilitate or impede the implementation process at the provider, health system, and patient levels.

We have used the Pragmatic-Explanatory Continuum Indicator Summary (PRECIS-2) model in planning the design and protocol development for this pragmatic effectiveness trial. (Loudon et al, 2015; <https://www.precis-2.org/>). This includes nine factors that characterize pragmatic trials: 1) eligibility, 2) recruitment, 3) setting, 4) organization, 5) flexibility: delivery, 6) flexibility: adherence, 7) follow-up, 8) primary outcome, and 9) primary analysis. Consistent with a pragmatic effectiveness trial, we will use broad eligibility criteria and automated recruitment methods, mobile and web-based delivery of the intervention in healthcare systems requiring minimal expertise and resources, intervention adherence promoted through digital and phone-based coaching support, minimal web-based follow-up assessments, primary outcome data that are relevant to participants (depression symptoms), and inclusion of all outcome data available for the two study arms.

We will assess outcomes through 6-months postpartum to test the following aims:

**Aim 1: To evaluate the local adoption, adaptation, implementation, and sustainment of MMB for Moms across participating healthcare systems.**

The RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance; [www.re-aim.org](http://www.re-aim.org)) model will be used to evaluate the success of efforts to scale up and sustain MMB for Moms. Metrics for the RE-AIM model will include the following. We also note that qualitative analyses will be used to determine the *reasons* for results on each of the following outcomes (e.g. reasons why participation is declined):

* Reach: The number and proportion of eligible patients outreached in the MMB for Moms group who a) enroll, and b) complete at least 4 sessions of the program (minimal dose shown to be effective), and their demographic characteristics, to assess representativeness of patient participants among those who are eligible.
* Effectiveness: effectiveness of MMB for Moms will be assessed as described in Aim 2.
* Adoption: The number and proportion of OB providers within and across each site who refer patients to MMB for Moms after the initial population-based recruitment phase for the trial is completed.
* Implementation: Frequency of patient participants’ use of the coaching support components of MMB for Moms across sites, as assessed by website usage statistics. This measure will also include the time and costs for study staff in responding to patient participants, as assessed in Aim 3.
* Maintenance: Individual level maintenance will be measured by improvements in depressive symptoms and relapse rates at 6-months postpartum, as described in Aim 2. Site level maintenance (i.e., the extent to which the program becomes part of routine care delivery) will be measured by the proportion of pregnant women across sites who are new users of the MMB for Moms program and not in the original trial cohort, as measured by website usage statistics.

**Aim 2: To test the hypotheses that pregnant women with histories of depression who participate in the MMB for Moms program will experience less depression (primary outcome), stress, and anxiety, better infant outcomes, and improved maternal function, compared to those who receive UC**, **and that these improvements will be robust across different patient racial and ethnic groups**.

Specific hypotheses are that, compared to the UC group, the MMB for Moms group will:

H1 (primary outcome): Report greater depressive symptom reduction post-intervention and at 6-months postpartum, based on the mean difference in PHQ-9 scores between groups.

H2 (primary outcome): Show lower rates of depressive relapse, based on the proportion of patients in each group with PHQ-9 scores >10 at 6-months postpartum.

H3 (exploratory outcomes): Report lower levels of stress and anxiety post-intervention and at 6-months postpartum, as assessed by mean group differences on the Perceived Stress Scale (PSS-10) scores and Generalized Anxiety Disorder scale (GAD7) scores, respectively.

H4 (exploratory outcomes): Have infants with higher mean gestational age at delivery, and lower rates of preterm birth and rates of small for gestational age (SGA), higher rates of attainment of developmental milestones based on results from the Ages and Stages questionnaire administered at 2 months postpartum.

H5 (exploratory outcomes): Report better maternal functioning, as assessed by lower scores on the Parenting Stress Index‐Short Form (PSI‐4/SF), and higher scores on the maternal Efficacy Questionnaire.

**AIM 3:** To test the hypothesis that MMB for Moms will demonstrate incremental cost effectiveness within willingness to pay thresholds, based on the health care system perspective. We will estimate the cost of delivering MMB for Moms, the total costs associated with MMB for Moms relative to UC, costs per participant, and the incremental cost per depression free days (DFDs) and quality adjusted life year (QALYs) over the 6 months postpartum period.

H1: The MMB for Moms group will demonstrate incremental cost-effectiveness relative to the UC group, defined as a lower marginal cost per additional number of DFDs for participants over the 6 months following the intervention.