Impact of perinatal depression treatment on child developmental outcomes (*acronym:* **SHARE-CHILD)**

Protocol submitted to the Committee on Ethics of Research on Human Beings

Human Development Research Foundation

NCT 02658994

April 15, 2016

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1. Background

Maternal depression is a serious disorder, which affects 20-30% women in low-income countries, is a known risk factor for impaired child development and long-lasting negative consequences on the child. Specifically, the increased risk of mental health problems in the child persists over the life course and is again transmitted to the next generation. The degree to which they causally shift the child's socio-emotional, cognitive, and physical development trajectory is less well understood.

The purpose of our project is to examine whether the successful perinatal depression intervention among mothers leads to improved developmental outcomes in the children from 3 months to 36 months.

2. Aims & Objectives

SHARE CHILD will be nested within an ongoing research program i.e. SHARE- THPP (Thinking Healthy Program delivered by peer volunteers), spearheaded by SHARE (the South Asian Hub for Advocacy, Research and Education on mental health).

SHARE is a collaborative network that is composed of the following: Human Development Research Foundation (Pakistan); Health Services Academy(Pakistan); Institute of Psychiatry (Pakistan); London School of Hygiene and Tropical Medicine and Institute of Psychiatry (UK); University of Liverpool (UK); Public Health Foundation India (India); Sangath (India); Johns Hopkins Bloomberg School of Public Health (US); And a dozen of network of NGOs spread across India, Afghanistan, Nepal, Bangladesh and Sri Lanka.

The broad, long range goal of SHARE is to establish a collaborative network of institutions in South Asia, to carry out and to utilize research that answers policy relevant questions related to reducing the treatment gap for mental disorders in the region. SHARE aims to be a driver to facilitate evidence-based mental health policy and program implementation in one of the world's most populous regions with weak health systems and poor social development indicators.

As a result of this collaborative network currently HDRF in partnership Sangath (India) are to implement an RCT (Randomized Control Trial) study coined "SHARE – THPP (Thinking Healthy Program implemented by peer volunteers)."

The goal of this study is to rigorously evaluate the impact of SHARE THPP perinatal depression intervention delivered by peers that starts prenatally and continues through 6 months post-partum, on child development. We will achieve this by conducting a cohort study that is integrated with the intervention clustered RCT, also being implemented by HDRF.

The SHARE THPP includes individual and community-wide components and follows mothers with prenatal depression until 6 months postpartum. Our project, SHARE CHILD, builds on this trial in several critical ways. We (1) focus on child outcomes, (2) extend follow-up to 36 months postpartum, and (3) investigate factors that mediate and modify the effect of the intervention on child outcomes. A unique

window of opportunity is made possible due to the summer 2014 enrollment start date of the SHARE trial.

In addition to enrolling the depressed women who will participate in the SHARE trial, we will also enroll a control group of non-depressed women, and follow-up the mother-child dyads for at least 36 months post-partum. Enrolling the non-depressed mothers enables us to determine the extent to which the intervention can lead to equivalence between the treated depressed and non-depressed groups as well as to identify potential positive externalities to non-depressed women in the intervention arm.

The overall goal of the project is to follow-up families that participated in the SHARE THPP intervention and see whether the intervention has a positive impact on the cognitive and socioemotional development of their children. This larger goal can be broken down into the following objectives:

1. Enroll SHARE THP study participants and perinatally non-depressed women.

2. Assess developmental outcomes together with potential mediators and moderators up to 36 months.

3. Identify effect size of SHARE THPP intervention on child development and disseminate findings.

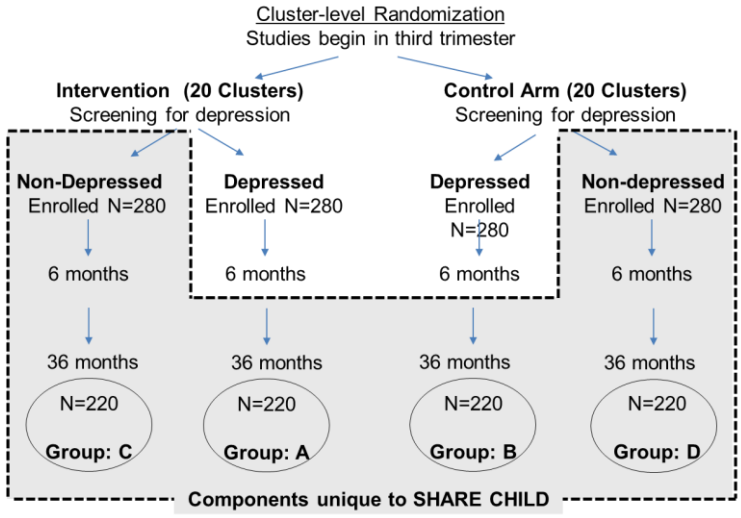
3. Methodology

3.1 Study Duration & Area

The total duration of the project will be 5 years (starting in April 2014 till April 2019). The study area will be Kallar Syedan, one of the 7 sub-districts of the District Rawalpindi, Pakistan.

The study population is based in rural and peri-urban areas in Rawalpindi, Pakistan. Eligible participants will be women between 16-40 years old, married, in their last trimester of pregnancy and intending to reside in the area for the duration of the study. The intervention utilizes a cluster RCT design with randomization at the Union Council level (administrative unit of approximately 2,500 people). Twenty clusters each will be randomized to the intervention and control arms. The two arms will be further subdivided into non-depressed and depressed women to yield four arms. Our target is to enroll 280 women in each of the four study arms (1,120 mother-child dyads total) and then follow them regularly until the child is 36 months of age. Due to attrition and loss to follow-up, we anticipate that 220 mother-child dyads in each of the four arms will complete the study. Total anticipated enrollment will be 1,120 (see Figure 1).

Figure 1. SHARE CHILD study design in relation to the Parent RCT Intervention. N=mother-child dyad. Shaded area unique to SHARE CHILD study.



The sampling unit within each cluster is the mother-child dyad. Women in the last trimester of pregnancy residing in one of the 40 study clusters will be identified through community surveillance normally conducted by community health workers (CHW). CHWs are utilized in most lower/middle income countries to deliver basic maternal and child health services. In Pakistan, each CHW covers 100 households and is informed of every pregnancy. Our research team has a long-standing relationship with the CHWs in the study areas. The CHWs will liaise with the research field staff which will seek informed consent from the pregnant woman and screen her for depression using the PHQ-9. We will offer enrollment to each woman who screens positive for depression and the first woman who subsequently screens negative. As a result, every cluster in the intervention and control arms will include women who score above and below the depression screening cutoff. Due to the community nature of the intervention, we anticipate that non-depressed women in the intervention clusters will benefit from the trial. Women who are suicidal, psychotic or already under depression treatment will be referred to mental health specialist care and excluded from the study. If the infant is born with congenital abnormalities or with other significant health problems, the mother-child dyad will be excluded.

Our data collection protocols that begin prenatally through 6 months postpartum will be synchronized with the main SHARE study (see Figure 1). After 6 months, SHARE ends and we continue the SHARE CHILD data collection. Interviews will be scheduled at 3, 6, 12, 24 and 36 postpartum month milestones for each mother-child dyad (see Table 1).

Table 1: Timeline of SHARE CHILD assessments

Breastfeeding		✓	✓	✓		
MSPSS	✓	✓	✓	✓	✓	✓
PHQ-9	✓	✓	✓			
WHO-DAS	✓	✓	✓			
Sociodemographic questions	✓			✓	✓	✓
BAYLEY				✓	✓	✓
HOME		✓	✓	✓	✓	✓
ASQ SE			✓	✓	✓	✓
Vineland			✓	✓	✓	✓
Height/Weight		✓	✓	✓	✓	✓
Maternal postnatal attachment		✓	✓			
Maternal efficacy		✓	✓			
Cohen PSS		✓	✓	✓	✓	✓
IPV	✓	✓		✓	✓	✓
CISR		✓	✓			✓
SDQ						✓
Risk game	✓			✓		
Stroop test	✓			✓		
Autonomy questions	✓			✓	✓	✓
A day in life		✓	✓			
Father involvement in child care	✓	✓	✓	✓	✓	✓

3.2 Data Management

Five bachelor/masters' level behavioral scientists or psychologists will be employed jointly by the SHARE and SHARE CHILD studies to conduct all interviews under the direct supervision of Dr. Siham Sikander, PI of the Pakistan site. These interviewers will receive extensive initial and ongoing training. Enrolled mothers will not be blind to depression status or intervention arm; interviewers will be blind and families will be instructed not to disclose maternal depression or intervention status.

Depression will be assessed through the Revised Clinical Interview Schedule (CIS-R).55 The CIS-R is a gold standard instrument for assessing psychopathology in community settings and has been widely used in both rich and poor countries. It assesses 14 non-psychotic symptoms that can be mapped to ICD-10 diagnoses. In addition, functional limitations related to mental health at all time points will be assessed with the World Health Organization Disability Assessment Schedule (WHO-DAS).

Confidentiality of all data collected will be maintained at all times. All the data from individuals will be given codes to ensure anonymity, that is mother-infant pairs will be identified by unique ID numbers. All questionnaires, handwritten field notes, transcripts and tape recordings will be kept securely.
The database of the SHARE CHILD will be stored on computers, which are security protected, with password access only by senior project staff. Data will be kept confidential and accessible only to the senior project staff.

3.3 Description of Measures

Socio-emotional development
At the 36 month time point, we will rely on the Strengths and Difficulties Questionnaire (SDQ). The SDQ is the most frequently used tool for assessing child behavior in LMIC and is highly correlated with longer scales, e.g. the Child Behavior Checklist. The SDQ is a parent report of 25 child attributes divided into five subscales: emotional symptoms, conduct problems, hyperactivity, peer problems, and prosocial behavior. We will also include an examiner report of child behavior as observed during the interview and cognitive assessment using the Behavior Observation Inventory from the Bayley Scales of Infant Development.

The Socio emotional part of Ages and Stages Questionnaire (ASQ SE) will be used to measure the socio emotional development of the child starting at 6 months of age. Interpersonal relationships, play, and leisure time and coping skills will be assessed using the Vineland Social-Emotional Early Childhood Scale. These scales are a combination of parent report and observer noted.

Cognitive development
We will use the Bayley Scales of Infant Development to measures the major areas of development including cognitive, language, motor, and adaptive functioning of the toddlers at 36 months of age. During the 6, 12, 24, and 36 month assessments we will assess child development with the Ages and Stages Questionnaire (ASQ). The ASQ is a widely used, simple set of 30 questions appropriate for 4–60-month-olds that assesses five domains of development: fine motor skills, gross motor skills, communication skills, problem-solving and personal-social skills. We will assess all five domains. Parents are asked to report age-appropriate milestones with the help of simple examiner administered examples, such as whether, at 8 months, the child plays with a toy by banging it up or down on the floor or table. The use of pictures is an especially good feature of the ASQ.

Physical development will be assessed using weight-for-age and height-for-age. Weight-for-age is sensitive to weight change over a short time period but fails to distinguish tall, thin children from those who are short with adequate weight. Height-for-age is more useful for identifying children with short stature, a group often exposed to longer-term adverse conditions. Head circumference will be used through 24 months. Based on WHO norms, a measure of 2 standard deviations below the mean is chosen to indicate delay. Physical health indicators are recent diarrheal episodes and acute respiratory infections.

3.5 Similar Research

As mentioned above the relevance of the current project it is important to note that there is no published study evaluating the impact of a peer delivered perinatal depression intervention on child development outcomes. The project is also significant in its implications for public health: If the study

demonstrates a positive impact of the intervention on child outcomes, it will provide a major impetus to policy-makers and health-planners to address maternal depression in early child development strategies. The intervention, which is designed to be integrated into existing maternal and child health programs, and delivered by non-specialists, would provide a sustainable model for replication in other settings.

4. Dissemination and Utilization of Results

The research has the potential to make a major contribution to advancing our knowledge of the extent and manner by which an intervention to treat perinatal depression will improve outcomes for children. This study combines rigorous research designs built upon the extensive expertise of the investigators. By evaluating this type of task-shifting intervention in a South Asian setting with a high prevalence of perinatal depression, the knowledge gained could be instrumental in influencing the mental and maternal health policy agenda in the region.

5. Ethical Considerations

A support letter will be obtained from the Pakistan Ministry of Health. Ethical approvals will be obtained from the Duke Institutional Review Board (IRB). Written informed consent will be obtained from each participant before they participate. The participant will be given a written consent form prepared in Urdu. Any questions will be answered by the research team member conducting the interviews. If the participant agrees, she will sign the consent form. Participants may withdraw from the study at any time. Hard copy and electronic information will be kept confidential by storing the data in a locked file cabinet and on an encrypted/password protected devices, respectively. We will not share information with anyone outside of the project team.

Any study participant who needs specialist mental health care will be referred to centers; referral procedures are already in place through local partner institutions providing specialist mental health clinical care. Those needing general medical care will be referred to local health units and the concerned medical officer and community health worker will be informed by phone and/or a referral letter. Both control and intervention community health workers will be trained to recognize life-threatening or serious conditions and take appropriate action.

6. Annexes

6.1 Information Sheet

6.2 Consent Form

6.3 CV of PIs