Official Title: **S**tudy to **U**nderstand **R**isk and **R**esilience **O**pportunity for **U**nder-resourced **N**ewborns after **D**elivery (**Project S.U.R.R.O.U.N.D.**)

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Study to **U**nderstand **R**isk and **R**esilience **O**pportunity for **U**nder-resourced **N**ewborns after **D**elivery (**Project S.U.R.R.O.U.N.D.**)

Centers for Innovation in Child Maltreatment Policy, Research, and Training (CICM)

Capstone Centers Grant: Project 3 – Phase 3 (RCT)

Principal Investigator:

Mini Tandon, D.O.

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A Introduction

A1 Study Abstract - Childhood maltreatment (CM) has highly deleterious effects on human development and is arguably the most influential, preventable cause of enduring psychopathology in the U.S. Infants and young children are at particularly high risk for physical harm from abuse and neglect, comprising over 60% of all child maltreatment fatalities. An increasing number of studies point to the ability to target prevention of CM by estimating individual-specific risk at the time of birth, on the basis of readily-available variables in birth records. The prospect of real-time identification of newborns at risk for CM on the basis of risk indicators available in obstetrical settings to be able to target prevention is exciting, but empirical testing of feasibility and predictive utility of methods are key to any systematic attempt to integrate this in U.S. obstetric or newborn clinical services. For example, birth record indices still identify a substantial number of children who do not go on to experience CM, making it important to attempt to optimize specificity (preserving sensitivity) with additional brief clinical screens or administrative data predictive risk modeling prior to broad implementation. Moreover, since screening is only as valuable as its actionability, it is important to understand whether screening results in uptake of needed preventive intervention and, in turn, whether this decreases actual CM.

In Phase I, we recruit a sample of 400 families enriched for risk for future CM, and contrast the performance of three types of newborn screening for risk of future official-report of CM involving: a) birth record risk variables (BRRV) only; b) BRRV plus a brief childhood trauma screen using the Childhood Trauma Questionnaire (CTQ), and/or current intimate partner violence; and c) retrieval and analysis of a set of medical record and insurance claims variables (for each family) based on those included in a large-scale Predictive Risk-Modeling (PRM) effort of a separate Capstone center project during the study period.

In Phase II, we ascertain information on familial risk for psychopathology as an additional risk parameter and obtain consent to cross-reference individual identifiers of enrollees with Official Report Maltreatment data from administrative records of the Missouri Department of Social Services. We are requesting dates of maltreatment reports, type of maltreatment reported, response type (assessment or investigation) and disposition (i.e. substantiated, unsubstantiated but need for services, assess and need for services, etc.).

In Phase III, we conduct a Randomized Control Trial (RCT) involving a risk-enhanced cohort of 150 of the subjects to explore the extent to which a brief, personalized education protocol for the primary caregiver enhances his/her engagement in intervention over care as usual. We will first determine whether this protocol enhances participation in recommended preventive interventions, and next explore whether CM report is reduced among participants randomized to the intervention arm.

In our initial request for review, we sought approval for Phases I and II, and approval was granted [HRPO #201811018]. **This protocol applies to Phase III.**

Phase III is a clinical trial that includes randomization into an intervention arm of tailored and enhanced education of parents regarding opportunities for interventions that are specifically keyed to the risk identified for their own family, and a control arm that

involves care as usual (referral to resources in general). This aspect of the program is being formally registered as an NIH Clinical Trial.

A2 Primary Hypothesis – Personalized education regarding clinical and community supports keyed to the individual needs of each family will a) increase participation in preventive intervention and b) reduce the occurrence of child maltreatment.

A3 Purpose of the Study Protocol - The project responds to several priorities of the Capstone RFA (RFA-HD-18-012) as well as the mission of Center for Innovation in Child Maltreatment Policy, Research, and Training to prevent CM and promote healthy development of victims of abuse and neglect.

B Background:

B1 Prior Literature and Studies - An increasing number of studies point to the ability to target prevention of CM by estimating individual-specific risk at the time of birth, on the basis of readily-available variables in birth records (e.g., marital and insurance status, birthweight, number of siblings, maternal age and education, smoking, and respective histories of prenatal care and abortion). Among 189,055 children born in Florida in 1996, Wu and colleagues (2004) demonstrated that half of all instances of early childhood maltreatment in this cohort occurred in 13% of the population that possessed a count of three or more risk variables from this list. Putnam-Hornstein and Needell (2011) replicated this observation in a California birth cohort of 531,035 births, demonstrating that among families with all the above risk factors present, 89% of the children had official-reports of CM in the first five years of life.

B2 Rationale for this Study - This clinical trial is a randomized controlled trial embedded within a prospective longitudinal study, in which families of infants recruited prenatally or in the newborn period are randomized to an enhanced level of resource navigation and engagement, which we refer to as PERCCS (Personalized Education Regarding Clinical and Community Supports). The enhancement involves keying recommendations for evidence-informed interventions for the prevention of CM to risk factors endorsed by the families themselves.

C Study Objectives

C1 Aim of RCT –We will determine whether PERCCS results in reductions in the occurrence of CM, through enhanced participation in preventive interventions keyed to the individual needs endorsed by families.

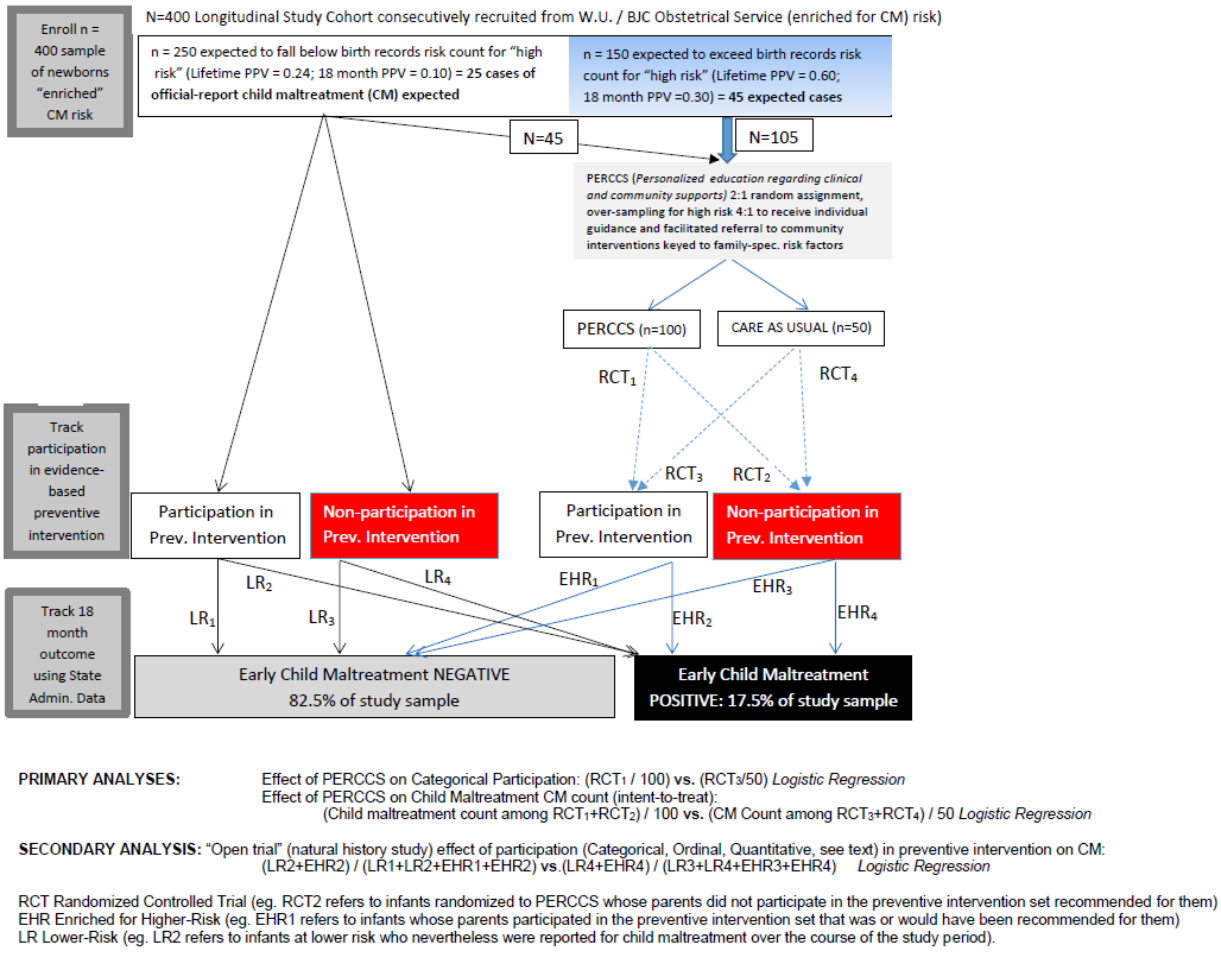
C2 Rationale for the Selection of Outcome Measures – Child maltreatment is a cause of enduring abnormalities of brain and behavioral development.

D Study Design

D1 Overview or Design Summary – The study design is summarized in Figure 1.

Infants are initially screened and risk levels ascertained according to the protocols specified in Phase I and Phase II of this research program. A risk-enhanced cohort of 150 of the infants will be randomized 2:1 to the PERCCS intervention. Details of PERCCS are provided in Tables 1 and 2. The timing of follow-up assessment (18 months) coincides with the lower end age threshold for reliable measures of early childhood psychopathology.

Figure 1. Schematic overview of study, including randomized, controlled trial (RCT).



PRIMARY ANALYSES: Effect of PERCCS on Categorical Participation: (RCT_1 / 100) **vs.** (RCT_3/50) *Logistic Regression*
Effect of PERCCS on Child Maltreatment CM count (intent-to-treat):
(Child maltreatment count among RCT_1+RCT_2) / 100 **vs.** (CM Count among RCT_3+RCT_4) / 50 *Logistic Regression*

SECONDARY ANALYSIS: "Open trial" (natural history study) effect of participation (Categorical, Ordinal, Quantitative, see text) in preventive intervention on CM:
(LR2+EHR2) / (LR1+LR2+EHR1+EHR2) **vs.**(LR4+EHR4) / (LR3+LR4+EHR3+EHR4) *Logistic Regression*

RCT Randomized Controlled Trial (eg. RCT2 refers to infants randomized to PERCCS whose parents did not participate in the preventive intervention set recommended for them)
EHR Enriched for Higher-Risk (eg. EHR1 refers to infants whose parents participated in the preventive intervention set that was or would have been recommended for them)
LR Lower-Risk (eg. LR2 refers to infants at lower risk who nevertheless were reported for child maltreatment over the course of the study period).

D2 Subject Selection and Withdrawal

2.a Inclusion Criteria

Participants (n=150) will be recruited from the participant pool of the longitudinal study Project SURROuND [HRPO #201811018]. Participants must be in Phase I and II to be eligible for Phase III participation. 45 sex-matched subjects (in triples) from the low-risk pool and 105 sex-matched subjects (in triples) from the high risk pool will be randomized 2:1 to PERCCS. Child subjects will include only the newborn(s) in a family. Should there be more than two newborns we will include all newborn children.

2.b Exclusion Criteria

We will exclude all individuals who are not already enrolled in Phase I or II of our study. We will exclude infants with serious medical conditions that preclude gains on measures used in the study (such as Down's Syndrome) or children that are likely to have long stays in the NICU for medical reasons therefore making the study and undue burden on the family. Otherwise no other exclusion criteria exist. The study team will review exclusion cases on a case-by-case basis to determine if the participant meets exclusion criteria. Review of the rate of participant accrual and compliance with inclusion/exclusion criteria will occur weekly at PI/study staff meetings

during the recruitment phases of the project, to ensure that a sufficient number of participants are being enrolled and that they meet eligibility criteria and the targeted ethnic diversity goals outlined in the grant proposal (Targeted/Planned Enrollment Table). Dr.Tandon and all research study staff will be present at these meetings. This information will be reviewed with Dr. Jonson-Reid on a bi-weekly basis during the progress and safety meeting.

2.c Ethical Considerations

Because study procedures cannot continue if the caregiver becomes incarcerated, we will not contact caregivers who become prisoners during the study period. We will not recruit parents who are minors. Existing participants who have withdrawn will not be reapproached for participation in Phase III.

2.d Subject Recruitment Plans and Consent Process

Recruitment: Participants will be recruited from our pool of n=400 participants.

Phase III involves randomizing n=150 study participants into a clinical trial, to provide the possibility for families to receive an enhanced service referral protocol to PERCCS after the baseline screen. This randomization meets the NIH definition of a clinical trial and will provide personalized parent education and facilitated referral keyed to identified risks. Families that receive PERCCS will be asked to include a release to share the referral information with the infant's pediatrician so the physician is knowledgeable about intervention recommendations and can encourage participation at well child visits.

Consent:

We have modified our study delivery methods to include Zoom and phone capabilities. This is an important recognition, as we serve a highly vulnerable population, including participants with health conditions, and newborns with underdeveloped immune systems. As such, we feel it is our responsibility to limit potential exposure to COVID. We follow the university guidelines for research participation, meeting in social distanced and universally masked spaces when appropriate, and engaging in virtual research when in-person is either not permitted, or not optimal based on the family's unique needs.

During COVID:

Verbal consent will be obtained from each participant at entry into the study. Informed consent is obtained by the following process, via phone or zoom:

1. Study team member will email a copy of the consent from to the participant.
2. The participant and team member will review the study consent form.
3. Study staff will confirm the participant's understanding of the study and answer any questions the participant might have.
4. Study staff will sign consent form and document consent process.

When able to return to campus:

Written informed consent will be obtained from each participant at entry into the study. Informed consent is obtained by the following process:

1. The participant will be asked to review the study consent form.
2. Study staff will confirm the participant's understanding of the study and answer any questions the participant might have.
3. Once the participant demonstrates understanding of the study and agrees to participate in the study, the consent will be signed in the presence of study staff.

2.e Randomization Method and Blinding

Randomized Clinical Trial, Personalized Education Regarding Clinical and Community Supports (PERCCS): In addition to information services given to all families, PERCCS serves as a supplemental opportunity for families to learn more about supportive clinical and community services for which they are eligible, that are keyed to their unique set of risks, and that are both available in the community and well-known to the study team. Similar in approach to Project SEEK, (Millett, 2016) it involves i) a review *with the mother* of all risks ascertained in the context of their individual screening ii) an appraisal of which community and clinical interventions substantively respond to those risks and are available to the subject (on the basis of each individual subject's zip code, insurance, and eligibility for the interventions)— see table below, iii) facilitation of contact between the subject and the respective provider agencies to initiate enrollment; and iv) authorization for the research team to share the personalized risk profile and support recommendations with the infant's outpatient pediatrician / primary care provider. The engagement with the participant's clinical providers is limited to providing them with the participant's risk profile and resource navigation plan. The clinical trial is needed to understand whether such an approach is "acceptable" to families after birth (irrespective of an ongoing relationship with a pediatrician as in Project SEEK) and we include referrals to a broader range of resources than explored in prior published research (Millett, 2016). Participants will be randomized 2:1 PERCCS:Control, and the randomization will be within successive sets of three families who fall in either "high risk" counts (n=105) families for child maltreatment or "low risk" counts (n=45) families. The project data manager will create an array of random numbers in a file repository in RedCap, for assignment to individuals in the randomization process. When a family enrolls into Phase III, the data manager will log the family ID into the file. Every three consecutively-enrolled families will become a set within each respective group, high risk vs. low risk group , and depending on the value of the random number that is assigned, the two families assigned with larger value random numbers will be enrolled in the intervention arm, and the remaining one family enrolled in the "control" arm.

The study team is aware of the sensitive nature of screening questions, is experienced in screening for mental health risk, and will comprehensively ensure respect, cultural awareness, and monitoring of each family's response, through a standardized script that covers all contingencies of risk and indication for intervention. **The script is appended to this application. The attached script comprises the content of PERCCS, as the 'intervention' is the individualized resource navigation.**

After a participant consents to participate in Phase 3, the research team member would review each of their individual risk domains and the corresponding intervention. A sample simulation of four de-identified participants is included in this IRB submission. Each risk domain and corresponding intervention are color coded to help the research team member engage with the participant in a systematic method. Once the first risk domain and corresponding resource have been discussed, the research member would

move to the next risk domain.

The study team has a substantial history of research with vulnerable populations. All interviews will be conducted in private with the mother. In general, level of risk is framed to parents as falling into one of the following THREE DOMAINS: those that potentially interfere with the child's health and safety; those that interfere with parents' ability to maintain emotional availability; and those that impact parents' ability to consistently and appropriately respond to infants' needs for nurturing and developmental support.

The community and clinical supports responsive to specific risk factors are summarized in Table 1 below:

	Risk Variables	Intervention*	Cutoff Criteria
1	Birth abnormality	A,D	Any abnormal conditions of the newborn recorded in Birth Records
2	Low birthweight	A,D, E	Birthweight less than 2500g
3	Medicaid/uninsured	A,B,D, E	Has only Medicaid or is Uninsured
4	Adequacy of prenatal care	A, D, G	No prenatal care or did not start care until less than 3 months before baby was born
5	Single head of household	A, D, G	Not married to the newborn's father
6	Readiness to parent screen	A, D, G, H	Identification of Parents At Risk for child Abuse and Neglect (IPARAN) Score>=1
7	Number of living siblings	D, F, G	Total number of living children born to the mother >=3 (inclusive of the subject child's birth)
8	Closely spaced pregnancies	D, F, G	Pregnancy Interval less than 15 months
9	Unmet mental health/depression	D, A, C	Edinburgh Postnatal Depression Scale (EPDS) Score >=10, self-report history of mental illness
10	Prior history of childhood trauma	A, C, D, G	Scored positive on any 5 clinical scales of Childhood Trauma Questionnaire (CTQ)
11	Substance use (12 month)	B, D	Positive on either Alcohol or Drugs use screening, by National Institute on Drug Abuse (NIDA)
12	Intimate partner violence	B, C, D	Hurt, Insulted, Threatened with Harm and Screamed (HITS) score > 10
13	Unplanned pregnancy	A, D, F, G	Yes to unplanned pregnancy question
14	Maternal age at birth of the baby	A, D, G	Maternal age at birth of the baby < 25 yrs
15	Lack of high school diploma	A, D, G, I	Without High School Diploma or Vocational Certificate
16	Prior negative pregnancy outcome	D, F	Yes to previous abortion question
17	Smoking during pregnancy	D, J	Yes to smoking during pregnancy in Birth Records

	*Evidence-Based Intervention
A	Home Visitation
B	Case Management to Optimize Insurance Enrollment and/or Address Active Substance Use Disorder and/or Support Victims of Intimate Partner Violence
C	Parental Mental Health Treatment
D	Emergency / Crisis Services
E	Low Income Home Energy Assistance Program (LIHEAP)/WIC
F	Reproductive Health Planning
G	Parenting Education
H	Parent Cafes
I	Adult Education and Literacy
J	Tobacco Quitline

Control Group: The control group will be given access to the same resources as the PERCCS group, however there will be no individualization and no referral plan made based on the family's individual risks. Control group participants will be given a START HERE STL resource manual, a parent training manual, and the Project SURROuND brochure.

2.f Risks and Benefits

Potential Risks

Potential risks: It is possible that caregivers may perceive pressure to participate to please their clinical team or access services. Caregivers will be fully informed regarding the fact that participation in the study in no way impacts eligibility for other services. Because the interviewers are all mandated reporters of child maltreatment, there may also be some increased risk of a report due to heightened surveillance. Caregivers will be fully informed regarding the limits of confidentiality due to mandated reporting. Given the nature of the obstetric setting, it is less likely that this will occur at baseline. The experience of the study team, is that cases in which a report becomes necessary during the course of a planned interview are quite rare. Additionally, it is possible that the interventions we have identified, that correspond with the risks for child maltreatment, may not be readily available in the community. This may be due to a high demand, waitlists, ineligibility for some research participants, or closure due to community-wide influences [such as COVID-19].

Protections in place to manage risks:

1. For Phase III, subjects are informed they may find some of the questionnaire questions about their baby's social and emotional development to be difficult to answer. These are standard questions that we are asking of all participants in the study. Subjects are told that if any particular question does make them uncomfortable, they should feel free to discuss this with the Interviewer. Subjects will be instructed that they may choose not to answer any questions with which they still feel uncomfortable.

2. Phase III participants are informed that rare risks are associated with accidental confidentiality breach through (1) an accidental breach of confidentiality about a subject by a trained interviewer; (2) the loss of data collection forms with identifying information; or (3) a break-in to the project office by someone with knowledge of the information on the system and sufficient technological capacity to bypass the password safeguards and re-link the identifying information to the subject lists in a locked cabinet. These risks are minimized by the thorough training of interviewers, the significant supervision provided by the team and the multiple locks and passcodes required to obtain data once collected.

3. As a general rule, interviewers will not be allowed to take the interview responses or provider progress reports home. Data collected in the field must be returned to the project office and placed in a locked cabinet. In cases of extreme emergency, in which staff must work from home (i.e. COVID-19), all data materials will be locked in HIPAA compliant storage containers and returned to the office as soon as possible. After baseline interviews and screenings, subsequent instruments will be identified solely by use of the case ID rather than a participant name.

4. Prior to computerized data entry, all subjects will be assigned a project id that links, and identifying data will not be included in the computer database. There will be one computer used for data entry tasks and the Data Programmer's computer will be reserved for linking and storage of data. All computers are

password protected at the log-in and database levels. Identifying information is removed from the computer after data linkage is complete and identifying information kept in a locked cabinet.

5. Linked individual level data are not reported back to the partner agencies, meaning that the information cannot be used to sanction an individual—the events have also already occurred making such uses of the data even less likely. Great care is taken during the data acquisition and preparation process to ensure continued confidentiality of the identities of children and families involved in this study.

6. All research clinicians will be trained to assess suicidality and homicidality, including thoughts about harming the fetus or baby, and to take appropriate steps. For those who endorse suicidal ideation, severity of suicidal ideation will be assessed using the Scale for Suicidal Ideation (Beck, Kovacs, & Weissman, 1979), which assesses the extent of suicide risk (i.e. wish to live vs. die, plans, intent). The assessment should take between 2-5 minutes to complete. If a patient endorses suicidal ideation, intent, or plan, the clinician will follow an operationalized protocol developed to manage high-risk depressed participants in clinical research (Pearson et al., 2001). Our protocol is outlined in the Project SURROuND Protocol for EPDS [approved by the Washington University IRB and attached to this protocol]. Briefly, the protocol outlines that if the participant is located in the clinic, the enrolling study team member should contact study coordinator, to further evaluate the participant. If a patient endorses homicidal ideation, intent, or plan, the administering clinician will follow state protocol for duty to warn and seeking emergency mental health assistance for further evaluations and assessments. All clinicians will have cell phones and Dr. Tandon, or a designated on-call clinician, will be reachable at all times. In the unlikely case of extreme emergency, clinicians are instructed to call the university or hospital security team (if in the clinic) or 911 for immediate assistance. This plan, and its implications with respect to the need to balance safety with confidentiality and autonomy, will be explained to the participant at the time of consent. Suicidal attempts or hospitalizations are considered serious adverse events and are reported to the IRB as per their guidelines. Under no circumstances will a study team member personally transport a participant.

7. Community interventions will be evaluated and if they are unavailable due to reasons outside of our control, our clinicians will help the participant navigate the next available comparable resource. Major unavailability of a community resource will be documented and discussed with the research team.

8. The analyses for results, reports or publications are all conducted at a sufficiently aggregate level to avoid incidental identification of subjects due to rare combinations of factors or location. Only the data manager and the PI have access to the computer storing data, which is password protected at the terminal. Personal identifiers present in the data are stripped from the other information as soon as data are cleaned and linked. After data entry and analyses are completed, all records containing identifying information will be destroyed.

Potential Benefits

The subjects will be given the opportunity to access established community interventions for parenting, home visitation, psychiatric and substance use disorders, and other resources that are available through collaborative networks of providers affiliated with CICM. These services may help prevent maltreatment and also address other risk factors facing the family. After the 18-month interview, if the child measures indicate concern in normative physical or behavioral development, Phase III families will be provided with assistance in accessing services specific to those needs by being selected to participate in the PERCCS randomized control clinical trial. Drs. Tandon and Rogers are extremely knowledgeable about clinical services available to address early signs of psychopathology. The opportunity to avoid maltreatment from ever occurring in families is a direct benefit to subjects, infants, communities, and has implications for lifelong wellness. Families will also receive children's books at each interview and reminders of well-child visit schedules during interim tracking and check-in calls. Subjects may benefit from the time they dedicate and the opportunity to add to the science and understanding of maltreatment risk pathways. As mentioned earlier, some subjects may perceive benefit from the study participation itself; vulnerable subjects have been found to report positive reactions to participation and belief that their participation was meaningful (Widom & Czaja, 2005).

2.g Early Withdrawal of Subjects

Subjects will be allowed to withdraw from the study at any time. There will be no negative consequences and will not impact their continuing services with their BJC clinical team or other primary care provider or child's pediatrician.

2.h When and How to Withdraw Subjects

Subjects can withdraw from the study at any time. They are instructed to contact project coordinator, Mackenzie Hynes at 314-532-0575 or Dr. Mini Tandon at 314-286-2302. Subjects may also send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

2.i Data Collection and Follow-up for Withdrawn Subjects

If a subject withdraws from the study we will ask for their permission to continue to contact them for participation in future phases of the study, depending on what phase they withdrew their participation. Should this occur we will ask the subject to sign a separate consent form before collecting this information. If a subject withdraws from the study, the research team may only use and share information already collected for the study. Subject information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.

E Study Procedures

E1 Screening for Eligibility

i All current study participants are eligible for participation in Phase III. Caregivers must have permanent custody (i.e., not a foster parent) and will be excluded if they have severe mental health disorders (e.g., psychotic disorders) or severe cognitive delay that diminishes their capacity to consent or effectively

participate in the study. If mothers express suicidal ideation, we will refer them for further evaluation immediately rather than proceed with consent for the study. Further, if they express concerns for their safety related to active IPV or their partners are present and refuse to allow them to participate in the screening alone, we will assist them as desired with referrals for services but not attempt to include in the study.

ii *Special classes of subjects*: The caregivers may be considered vulnerable due to socioeconomic status. It is impossible to assess the outcomes of the study without their inclusion. Several aspects of the study reduce concerns in this area: (1) we are drawing from a population receiving services as usual from BJC health system with skilled clinicians doing the initial screening and judgment about inclusion and exclusion, (2) the team has extensive research and clinical experience with vulnerable families with young children, (3) the study procedures are brief and designed to follow along with usual care well-baby checks to reduce any burden. Finally, all families will receive usual care referral sheets to services

E2 Schedule of Data Collection

Our data collection and subject tracking plans are limited to tracking actively engaged services by participnts, including the duration and frequency of the intervention.

E3 Safety and Adverse Events

3.a Safety and Compliance Monitoring

Study Identification Information:
NIH Study Number: P50 HD096719
Principal Investigator (PI): Mini Tandon, DO

The Data Safety Monitoring Plan (DSMP) outlined below will adhere to the protocol approved by the NICHD and the Washington University IRB. This is a single-site study. Dr. Tandon will be the primary monitoring entity. She will have primary responsibility for the monitoring of participants during the entire time they participate in the study, both with respect to their safety (including confidentiality) and the integrity of their research data.

3.b Definitions of Adverse Events

An adverse event (AE) is any untoward medical occurrence in a participant temporally associated with participation in the clinical study or with use of the experimental agent being studied. An adverse finding can include a sign, symptom, abnormal assessment (laboratory test value, vital signs, electrocardiogram finding, etc.), or any combination of these.

A Serious Adverse Event (SAE) is any adverse event that results in one or more of the following outcomes:

- Death
- A life-threatening event
- Inpatient hospitalization or prolongation of existing hospitalization

- A persistent or significant disability/incapacity
- A congenital anomaly or birth defect
- Important medical event based upon appropriate medical judgment

3.d. Classification of Events

i **Severity -** The most serious risk in the proposed research is any adverse outcome that may jeopardize the welfare of participating infants or caregivers. AEs will be labeled according to severity, which is based on their impact on the patient. An AE will be termed “mild” if it does not have a major impact on the patient, “moderate” if it causes the patient some minor inconvenience, and “severe” if it causes a substantial disruption to the patient’s well-being. AEs will be categorized according to the likelihood that they are related to the study intervention or other study procedures. Specifically, they will be labeled definitely unrelated, definitely related, probably related, or possibly related to the study intervention or procedures. Possible adverse events that are anticipated include the need to waive the confidentiality of the participants in the case that they express suicidal or homicidal ideation or intent, or child abuse.

ii **Expectedness -** Study assessments: The assessments to be conducted as part of this study are non-invasive and carry with them no more than minimal risk. The most significant risks to the participants related to assessments are those that would follow a breach of confidentiality and the disclosure of clinical information. PERCSS: Participants assigned to PERCSS may feel uncomfortable disclosing private and/or emotional experiences. This risk is minimized by using well-trained and supervised staff. Control Group: Participants assigned to the Control Group may also feel uncomfortable disclosing private and/or emotional experiences. This risk is minimized by using well-trained and supervised staff. Risks in relation to benefits: No participants will be denied interventions; participants receive either standard of care in the community or the PERCSS intervention. No risks other than possible emotional distress exist from the study assessments. Thus, the risks involved in participating in this study are deemed low, which justifies the data and safety monitoring plan described here.

3.e. Data Collection Procedures for Adverse Events

The PI will be responsible for monitoring participant safety at regularly scheduled research meetings. The PI will keep a written log of all adverse events and ensure that the IRB is contacted immediately and will also keep a log of the outcome of IRB decisions regarding adverse events and enforce any changes that need to occur as a result of the IRB decisions. If the preliminary outcome data indicates harmful impact of the program to caregivers or their families, the Washington University in St. Louis committee will be notified and it is possible that the study will be discontinued.

The PI and his staff will provide adequate safeguards for the protection of confidentiality of all research records. Procedures designed to maintain confidentially include: (1) training for all research staff emphasizing the importance of confidentiality; (2) specific procedures developed to protect participants’ confidentiality, and (3) formal mechanisms limiting access to information that can link data to individual participants. Data forms that

include identifying information will be kept in locked cabinets. Only the unique ID number, assigned by the research coordinator at the time of initial contact will represent participants during data entry, data transfer, data analysis, or other file management procedures. To facilitate tracking, a password-protected computer file will be maintained containing the identity of participants, their ID numbers, and information about how they can be reached. Only members of the investigative group will have access to secured files or to master lists for participant code numbers and will be well informed regarding the protection of patients' rights to confidentiality. Identities of participants will not be revealed in the publication or presentation of any results from this project.

All participant research data is stored separate from participant contact information, which is stored on our secure servers with network and database level passwords, only accessible to research staff who need contact with the participants.

Research staff and participants will provide data through paper and/or electronic forms. Tracking forms will document that procedures were followed and completed at each visit. A closed and password-protected data-entry system will track data in real time as they are entered. This will allow continuous checks on data completion and integrity (e.g., errors). Range checks, review screens, and error trapping routines will be built into the system as quality control procedures to minimize the chance of data entry errors. Hard copy data summaries of all active and recent participants will be provided to the PI who will review them for any apparent errors, missing data, or discrepancies. The frequency of this formal review of the integrity of the accumulating study data will be approximately weekly. This information will be reviewed with Dr. Tandon monthly, or more frequently if errors are detected.

3.f. Reporting Procedures

The PI will be informed of any AE as soon as they occur, and he will report them to the Washington University in St. Louis IRB within 24 hours of becoming aware of the event. AE reports and annual summaries will not include participant- or group-identifiable material. Each report will only include the identification code.The IRB will determine whether it is appropriate to stop the study protocol temporarily or will provide suggestions/modifications to the study procedures. Possible modifications include adding these possible adverse events to the consent form and re-consenting all study participants. Because this study is embedded within a center, the PI will also be responsible for notifying the center PI and steering committee.

Additionally, in accordance with NICHD policy, the PI will notify the study's NICHD program officer within 15 calendar days of the study team becoming aware of an unexpected serious adverse event (SAE). For all AEs or serious adverse events (SAE) that are either expected or unrelated to the study, the PI will provide a summary to the study's NICHD program officer with the annual progress report.

3.g. Adverse Events Reporting Period

AE reporting to the Washington University in St. Louis IRB will occur within 24 hours of becoming aware of the event. Additionally, in accordance with NICHD policy, the PI will notify the study's NICHD program officer within 15 calendar days of the study team becoming aware of an unexpected serious adverse event (SAE).

3.h. Post-Study Adverse Events

There are no anticipated post-study adverse events that would accrue from cross-referencing or analysis of research data since this information will not be returned to the family.

E4 Study Outcome Measurements and Ascertainment

If the preliminary outcome data indicates any harmful impact of participation in the program to caregivers or their families (this is extremely unlikely and we would anticipate that Phase I, II and III of this program would be designated low-risk), HRPO will be notified immediately.

F Statistical Plan

F1 *Statistical Analyses:*

i. Intent-to-treat analysis of impact of PERCCS on service utilization. We will calculate the total proportion of evidence-informed services indicated by risk profiles of all families within each group (the intervention group and the control group) and compare the groups using logistic regression methods

ii. Intent-to-treat analysis of the impact of PERCCS on the occurrence of child maltreatment. We will compare the rate of official-report abuse/neglect between the groups using logistic regression methods

iii. (Secondary) We will conduct logistic regression analysis simultaneously examining the effects of risk count and service access on official report child maltreatment outcome.

The randomized controlled trial has adequate statistical power to detect an odds ratio of 2.0 for the effect of PERRCS in reducing child maltreatment outcome.

Additional analyses that pertains to Phase I and Phase II are detailed in the protocols for those respective phases of the study.

F2 ***Interim Monitoring and Early Stopping -*** In the case of an adverse psychological reaction to the acquisition of interview data, a standard protocol will be followed. This protocol consists of providing mental health support to the subject, and in cases in there is any risk of harm to self or others by the subject, contacting 911 immediately and notifying any explicitly identified victims. Additionally, if the team has to report maltreatment which results in a child being taken into custody by child welfare, there will be no attempt to enroll the child in any successive phase of the study.

The Principal Investigator and all co-investigators on the team are mandated reporters and are trained regarding the limits of confidentiality and to err on the side of caution in the event of the need to break confidentiality due to mandatory reporting of imminent risk of harm to a child. The PI has been trained either to

contact the police to ensure the safety of participants, or if appropriate, to have emergency personnel take the family member to the nearest emergency room.

F3 ***Statistical Methods –*** see above

F4 ***Missing Outcome Data***

N/A—an advantage of utilizing state administrative data as an outcome parameter is that it affords complete ascertainment

F5 ***Unblinding Procedures –*** N/A

G Data Handling and Record Keeping

G1 ***Confidentiality and Security -*** To help protect participant confidentiality, we will de-identify all information obtained; it will immediately be given a code number. A master list linking the code number to the participant's identifiers will be kept separate from the research data. Only the Principal Investigator and our trained staff will be able to see the list. The offices of the PI are locked when unoccupied and the building is both locked when not in operation and is patrolled 24 hours a day by the Washington University School of Medicine campus security team. Questionnaires with identifying content are stored with a two door lock system. All data will be stored on WU servers that are behind firewalls that meet/exceed HIPAA requirements for protecting PHI. Data will be entered on password protected computers and immediately moved to the servers upon completion. No data from this study will be saved on the hard-drive of a staff member's computer. Any information shared will be de-identified except as necessary for the reasons stated above. Any report or article that we write will not include information that can directly identify the participant. The journals that publish these reports or articles require that we share participant information that was collected for this study with others. Sharing this information will allow others to make sure the results of this study are correct and help develop new ideas for research. Participant information will be shared in a way that cannot directly identify them.

To further protect participant privacy, the researchers have obtained a Certificate of Confidentiality from federal government. This means that the researchers can refuse to disclose information that may identify subject in any legal or court proceeding or to anyone who is not connected with the research except if:

- there is a law that requires disclosure, such as to report child abuse and neglect, or harm to self or others*;*
- subject gives permission to disclose their information, including as described in the consent form; or
- it is used for other scientific research allowed by federal law.

Subjects have the right to share their information or involvement in this study with anyone at any time. They may also give the research team permission to disclose their information to a third party or any other person not connected with the research.

Protected Health Information (PHI) is health information that identifies a participant. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, participants must give the research team permission to use and disclose (share) their PHI for the study as explained in the consent form. The research team will follow state and federal laws and may share their health information with the agencies and people listed in the consent document in the section titled, "How will you keep my information confidential?" Once health information is shared with someone outside of the research team, it may no longer be protected by HIPAA. The research team will only use and share participant information as talked about in the consent form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to the participant(de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in the consent form. If participants have questions or concerns about their privacy and the use of their PHI, they are instructed to contact the University's Privacy Officer.

Although they will not be allowed to see the study information, participants may be given access to their health care records by contacting their health care provider.

G2 ***Training -*** In accordance with the October 1, 2000, NIH policy, all key personnel involved in the design and conduct of the human subjects research aspect of this grant have been (or will be) educated in the protection of human research participants. Washington University's Web-Based Instruction on Conducting Human Research is an interactive web-based program that provides information on conducting human research and the informed consent process. The Human Subjects Research Module includes developmental landmarks, current regulations, IRBs, informed consent, PI responsibilities, and study documentation; and a Research Integrity Module, which includes the traditions of science, responsible conduct of research, responsible authorship and publication practices, data, mentoring, conflict of interest, and PI responsibilities and research misconduct.

G3 ***Records Retention –*** Research records will be retained for 5 years following the conclusion of the study, then destroyed, with the exception of retention of an electronic data set, for which caregivers will be asked (in Phase III) to authorize future contact for the purpose of long-term follow-up.

G4 ***Performance Monitoring –*** The primary endpoints for performance monitoring involve targeted enrollment, which will be reviewed quarterly, and representation of the sample with respect to the risk variables described in this protocol. Enrollment counts for families that fall into each targeted enrollment category will be reviewed quarterly.

H Study Monitoring, Auditing, and Inspecting

H1 ***Study Monitoring Plan -*** The Principal Investigator will provide overall monitoring of the data collection, interviewer, participants, and data safety

throughout the study process. The Project Coordinator will also assist in the monitoring and supervision of data collection and will check in with advisors from the juvenile court at bimonthly project progress meetings. Any special needs uncovered will be immediately reported to the PI who will involve other team members as appropriate in handling any issue uncovered.

University and NICHD guidelines will be followed for reporting should an adverse event occur. Monitoring will include checking to see that data files are appropriately stored and bi-weekly group supervision of field interview staff to discuss the process, answer questions and provide assistance when needed. The project will also undergo review and approval by our Institutional Review Board with monitoring as required by annual reports and recertification of human subjects approval. The Data Safety Monitoring Plan is attached to this protocol and will serve as the protocol for adverse events [a summary is outlined under the adverse events portion of this protocol].

H2 Auditing and Inspecting - The project coordinator and data manager will provide random audits of data to ensure proper data management and confidentiality.

H3 Organization and Participating Centers – This Washington University Study will involve patients recruited from the obstetrical and newborn medical services of the BJC Health System, for which there is a strong long-standing affiliation agreement.

H4 Funding Source and Conflicts of Interest - The National Institute of Child Health and Human Development (NICHD) is funding this research study as well as institutional funds. This means that Washington University is receiving payments from NICHD to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from NICHD for conducting this study.

H5 Committees – N/A

H6 Subject Stipends or Payments

Phase III: Participants will receive a $30 gift card for their time participating in Phase III.

H7 Study Timetable – Participants will be engaged in Phase III until their child is 18 months of age.

I Publication Plan

Any report or article that we write will not include information that can directly identify the participant. The journals that publish these reports or articles require that we share participant information that was collected for this study with others. Sharing this information will allow others to make sure the results of this study are correct and help develop new ideas for research. Participant information will be shared in a way that cannot directly identify them.

J Attachments

J1 Figures and tables Attached

J2 Informed consent document Attached

J3 Special procedures protocols N/A

K References

1. Constantino, J.N. (2016). Child Maltreatment Prevention and the Scope of Child and Adolescent Psychiatry. *Child & Adolescent Psychiatric Clinics of North America*. *25*(2), 157-65.
2. Millett, L. Ben-David, V., Jonson-Reid, M., Echele, G., & Moussette, P. (2016) Understanding change among multi-problem families: Learnings from a long-term intervention program. *Evaluation and Program Planning. 58*, 176-183.
3. Parrish, J. W., Young, M. B., Perham-Hester, K. A., & Gessner, B. D. (2011). Identifying risk factors for child maltreatment in Alaska: A population-based approach. *American Journal of Preventive Medicine*, *40*(6), 666-673.
4. Putnam-Hornstein, E., & Needell, B. (2011). Predictors of child protective service contact between birth and age five: An examination of California's 2002 birth cohort. *Children and Youth Services Review*, 33(8), 1337-1344.
5. Widom, C., & Czaja, S. (2005) Reactions to Research Participation in Vulnerable Subgroups, Accountability in Research, 12:2, 115-138, DOI: 10.1080/08989620590957193
6. Wu, S. S., Ma, C. X., Carter, R. L., Ariet, M., Feaver, E. A., Resnick, M. B., & Roth, J. (2004). Risk factors for infant maltreatment: a population-based study. *Child Abuse & Neglect*, *28*(12), 1253-1264.