Title: **Early Literacy Promotion Among Poor Urban Children in Philadelphia**

Short Title ELP for Urban Children

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ABBREVIATIONS AND DEFINITIONS OF TERMS

ROR	Reach Out and Read
ACE	Adverse Childhood Experiences
SAHL	Short Assessment of Health Literacy
EPDS	Edinburgh Postnatal Depression Scale
ELP	Early Literacy Promotion
SLP	Standard Literacy Promotion
StimQ	Measure of Cognitive Stimulation Provided in the Home
PLS	Preschool Language Scale – 5th Edition
ITSEA	Infant Toddler Social Emotional Assessment
PHQ-9	Patient Health Questionnaire-9
PSI	Parenting Stress Index

ABSTRACT

Context:

Early childhood is a critical period in which young children attain developmental skills necessary for language function. Urban children continue to be at increased risk for language and cognitive delays. Such delays can lead to disparities in educational outcomes when compared to children from middle and upper income strata. Poor children including those who have participated in programs like Reach Out and Read still demonstrate language outcomes below national averages. Efforts to encourage parent child verbal communication earlier may be needed to address this gap. Initiating ROR prior to a child's 6 month well child visit may be more effective in improving language outcomes than waiting until 6 months of age to initiate this intervention.

Epigenetic pathways have shown how exposure to chronic stress from adversity leads to altered neurological development and cognitive impairment. This altered development can influence a parent's ability to be able to parent and nurture their children. Understanding the role that adversity and other individual, family, and neighborhood characteristics influence a parent's ability to read to their young children could provide additional areas to address within literacy promotion.

Objectives:

1) To test and determine the effectiveness of an early literacy promotion program compared to the standard literacy promotion on language development among urban children in Philadelphia.

2) To explore whether Parent history of adversity, health literacy, parenting stress, and depression moderate the effects of early literacy promotion.

3) To explore whether the effects of early literacy promotion are mediated through the intensity of reading behaviors.

4) To identify perceptions of barriers to and promoters of reading behavior among parents with high ACE scores.

5) To explore the effects of an early literacy promotion program compared to standard literacy promotion on social-emotional development among poor urban children in Philadelphia.

Study Design:

A randomized controlled trial will be conducted comparing two versions of the parent-child reading program: Early literacy promotion (ELP) and Standard Literacy promotion (SLP). An additional sub-study will utilize semi-structured interviews with a purposive number of parents enrolled in the study to explore barriers and promoters to reading to their children.

Setting/Participants:

We will recruit participants who are English or Spanish speakers, at least 15 years old, the parent of a child born ≥35 weeks gestation age and < 4 weeks at enrollment and with Medicaid insurance. We will be recruiting from one urban site affiliated with CHOP (Karabots). The combined total enrollment number of participants will be 240 (120 dyads of parent and infant). The target enrollment number of participants for the sub-study will be up to 30 parents.

Study Interventions and Measures:

In this intervention, parents/children randomized to the ELP arm will receive a book with developmentally appropriate advice about reading at each well child visit from one week through 5 months of age, as well as weekly text reminders related to reading. Those in the SLP arm will receive weekly text messages about child safety. From 6 months of age, both groups will receive SLP and will attend study visits every six months until age 2. Difference between the groups on the PLS (Pre-school language score-5th edition) score at 6 and 24 months of age are the main outcomes. StimQ score differences at 6,12,18, and 24 months of age will be a secondary outcome. Other outcomes include score differences at 12, 18, and 24 months in the PHQ-9 and the PSI-Short Form, and differences in the ITSEA at 18 and 24 months. A purposive sample of parents will participate in a qualitative interview component to understand barriers to reading, parents' perceptions of the value of reading to infants, and factors which promote reading.

1 BACKGROUND INFORMATION AND RATIONALE

1.1 Introduction

Poor urban children are at increased risk for language and cognitive delays. Such delays can lead to poor school readiness and disparities in educational outcomes when compared to children from middle and upper income strata. Reach Out and Read (ROR), a national program which promotes parent-child reading activities for children 6 months through 5 years of age at pediatric well child visits, has been shown to improve at-risk children's expressive and receptive language development. However, poor children who participate in ROR still demonstrate language outcomes that are below national averages. It isn't clear whether early literacy promotion, i.e. promotion of parent-child reading prior to six months of age, is more effective than standard literacy promotion and can further improve poor urban children's language and cognitive outcomes.

The disparities that continue to exist among language development despite literacy promotion efforts suggest that other barriers and factors may exist that influences these disparities. While it has been demonstrated that reading to infants is imperative for appropriate language development, the barriers and promoters to reading among low-income parents is not well understood.

1.2 Name and Description of Investigational Product or Intervention

The study intervention will be an adapted version of the Reach Out and Read (ROR) Program, a national program that promotes parent-child reading activities for children 6 months through 5 years of age at pediatric well child visits. It will be adapted for use with parents of children from two weeks to 6 months of age. Early literacy promotion will consist of the provision of developmentally appropriate books selected specifically for all well visits from one week of age onward It will also include text message reminders for the initial 24 weeks of the program to encourage best reading practices.

1.3 Relevant Literature and Data

Early childhood is a critical period in which young children attain developmental skills necessary for language function.[2] Early stimulation of brain centers involved in language development promotes critical neuronal connections leading to growth in language functioning. Unfortunately, language delays are common among children under age 3 years, particularly for children residing in impoverished communities.[3] The cause of these language delays are multifactorial but likely result from deficits in parent-child verbal interactions.[4] Twelve to sixteen percent of young children are estimated to have delays that affect language development.[5,6] Differences between poor and advantaged children in language processing skills and vocabulary are evident by 18 months of age.[7] These delays contribute to social and emotional problems and result in poor educational and functional outcomes.[8] Lifetime costs for individuals with developmental disabilities including language deficits has been estimated to exceed $60 billion in 2003 U.S. dollars.[9]

Parent-child reading represents an important source of language stimulation and is rich in verbal interactions that can stimulate language development.[10] Studies have found parent-child reading to be associated with improved language functioning and better school performance.[11-13] Based on this observation, the ROR Program was established to promote parent-child reading activity. ROR is based in pediatric clinical settings and provides developmentally appropriate books to young children and encourages a discussion of the importance of reading by pediatric clinicians at well child visits from 6 months through 5 years.[14] Evaluations of ROR have shown beneficial effects on reading activity and language outcomes.[15-17] These effects translate into an increase of 1 day/week of parent-child reading activity and a 4 to 9 point increase in expressive and receptive language scores respectively.[17] For this reason, the American Academy of

Pediatrics has recommended that pediatric clinicians promote early literacy development beginning in infancy.[18]

Despite these encouraging results, poor children who participate in ROR still demonstrate language scores that are 6 to 15 points lower than national averages.[17] This may be the result of delays in initiating parent-child verbal interactions until a child's 6-month well child visit. There may be reason to suspect that children exposed to more rich and intensive parent-child verbal interactions prior to six months of age may achieve greater language functioning and outcomes later on.[19,20] For this reason, we are proposing a study to test the effects of early literacy promotion beginning by 1 month of age with standard child literacy promotion using the ROR model beginning by 6 months of age.

Adverse childhood experiences (childhood adversity) have been shown to have significant impact on the life course of individuals including mental health, chronic disease, and even early death.[21-25] Examples of adversity include abuse, neglect, family dysfunction, and violence, among others. Exposure to adverse childhood experiences (ACE's) is frequent and significant in disadvantaged, minority communities.[26] Exposure to chronic stress from adversity leads to altered neurological development and cognitive impairment.[27-28] For many, adversity is chronic and continues into adulthood. A biological marker of stress is the level of cortisol. Through the measurement of cortisol levels, maternal stress has been shown to negatively impact infant cognitive development and infant-parent attachment.[29-30] For parents who have chronic exposure to stress and adversity, this likely can negatively impact their interactions with their children and through this mechanism also affect the development of their children.

Understanding how parents' exposure to ACE's influence reading behavior can inform the development of future early childhood development interventions that target communities with high exposure to adversity such as poor communities. Furthermore, understanding contextual factors that influence reading behaviors among parents can serve as additional areas to address in future literacy promotion interventions.

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. All episodes of noncompliance will be documented.

The investigators will perform the study in accordance with this protocol, will obtain consent and assent, 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

2.1 Primary Objective

The primary objective of the study is to test the effectiveness of early literacy promotion compared to standard literacy promotion among poor at-risk children.

Specific Aim 1: To determine the effectiveness of an early literacy promotion program compared to the standard literacy promotion on language development among poor urban children in Philadelphia.

2.2 Secondary Objectives

Specific Aim 2: To explore whether Parent history of adversity, health literacy, parenting stress, and depression moderate the effects of early literacy promotion.

Specific Aim 3: To explore whether the effects of early literacy promotion are mediated through the intensity of reading behaviors.

Specific Aim 4: To identify perceptions of barriers to and promoters of reading behavior among parents with high and low ACE scores.

Specific Aim 5: To explore the effects of an early literacy promotion program compared to standard literacy promotion on social-emotional development among poor urban children in Philadelphia.

Specific Aim 6: To explore the impact of early literacy on healthcare utilization

3 INVESTIGATIONAL PLAN

3.1 General Schema of Study Design

We propose to test the effects of early literacy promotion using a randomized controlled trial design. Eligible newborn children less than 1 month of age who present to Karabots Primary Care Center will be recruited and consented to participate in this two-year study. Children will be randomized to receive early literacy promotion or standard literacy promotion. Randomization sequences will be developed by the project biostatistician using computer-generated random numbers prior to study enrollment and will be placed in sealed opaque envelopes. Randomization will ensure equivalence between groups on measured and unmeasured characteristics and is considered to be the strongest protection against bias in study design.

Children randomized to the early literacy promotion arm will receive developmentally appropriate books and information on the importance of early parent-child reading activity by pediatric clinicians at well child visits from one week to 6 months of age, and weekly text message reminders concerning early literacy and daily reading activity up to 6 months of age. Developmentally appropriate books will be selected and standardized for each well child visit prior to 6 months of age (1 week, 1 month, 2 months, 4 months). Information on early literacy promotion will be standardized using a verbal script (Appendix 8) and will be provided to parents by pediatric clinicians at well visits prior to 6 months of age. The weekly text message reminders will be initiated following enrollment, will be standardized according to age, and will be scheduled according to parent preference in the morning, afternoon, or evening. The text message reminders will help remind parents to ensure that children in the intervention arm are exposed to parent-child reading activity in their first six months of life. Beginning with the 6-month well child visit, children in this arm will receive the standard ROR Program as described in the standard literacy promotion group below.

Children randomized to the standard literacy promotion arm will receive developmentally appropriate books and information on the importance of parent-child reading activity by pediatric clinicians beginning with the 6-month well child visit and weekly text message reminders concerning child safety. This conforms to the ROR National Program recommendations and is considered standard of care at these 3 urban clinics. To prevent contamination in which pediatric clinicians inadvertently provide books and instruction on reading activity to control children prior to 6 months of age, a research assistant will ensure that books and reading instruction are not provided to children in this arm prior to 6 months of age. The weekly text message reminders will be initiated following enrollment, will be standardized according to age, and will be scheduled according to parent preference in the morning, afternoon, or evening.

Children in both study arms will be followed every 6 months until age 2. Information on reading activities, expressive and receptive language outcomes, parental mental health, and child's social and emotional competencies will be collected in concert with scheduled well child visits. Differences in reading activities, parental mental health, childs social/emotional competencies, and language outcomes will be assessed between groups using intention-to-treat analysis.

A purposive sample of up to 30 parents of infant less than 6 months old who have consented to participate in the main study will additionally be recruited to participate in semi-structured interviews with aims to have an equal mixture of parents with high and low exposure to adversity. High adversity is defined for the purpose of this study as having an ACE score of 2 or greater. Low adversity is defined for the purpose of this study as having an ACE score less than 2. Parents with infants less than six months of age are specifically being targeted for the interviews to understand factors that affect this specific age group. The interviews will aim to explore and to understand barriers to reading, parents' perceptions of the value of reading to infants, and factors which promote reading in this population

3.1.1 Screening Phase

Children who attend these clinics are primarily poor (72% Medicaid) and diverse racially with 80% being African-American, 10% white, 5% Hispanic, and 5% Asian. Children will be eligible to participate in this study if they were born ≥35 weeks estimated gestational age, without neurodevelopmental disabilities or congenital malformations, with Medicaid insurance (proxy measure for poverty), and <30 days old at the time of enrollment. Children who are born premature <35 weeks EGA, who have neurodevelopmental disabilities, or who have congenital malformations are at increased risk of language delays and will be excluded. In addition, we will exclude families who do not speak English or Spanish, as the main measures of reading activity (StimQ, Appendix 6) and language development (Preschool Language Scale-V, Appendix 7) are only available in English and Spanish.

Potential subjects will be identified at the time of their first well child visit < 30 days of life using the electronic health record (EHR). Eligible newborns' parents will be approached at the time of their child's appointment by research staff. They will obtain written informed consent from participants in private. Participants will be randomized to receive either the early literacy promotion arm or the standard literacy promotion arm based on random assignment. Randomization sequences will be developed by the project biostatistician using computer-generated random numbers prior to study enrollment and will be placed in sealed opaque envelopes. Randomization will ensure equivalence between groups on measured and unmeasured characteristics and is considered to be the strongest protection against bias in study design. Written informed consent will be obtained prior to any study related procedures being performed in person. Consent will include a discussion of study rationale, procedures, measures, benefits, risks, and alternatives to participation. After consent, subjects will either be assigned to the literacy promotion arm or the standard literacy promotion arm of the study. Regardless of their assignment, once they have consented to participate, they will complete a demographic questionnaire (Appendix 1), questionnaires about adverse childhood experiences (Appendix 2), and health literacy (Appendix 3) and the Edinburgh Postnatal Depression Scale (EPDS) (Appendix 4) prior to the intervention.

Both parents with high and low ACE scores will be called to explain the qualitative component of the study and to see if they may be interested in participating. Those who agree to participate will be scheduled at Karabots for an in-person interview. For participants who fail to present more than 2 times for an interview, a phone interview will be offered. For those participating in an-in person interview, additional written informed consent will be obtained at time of the interview. For those that an interview is conducted via the phone, a written consent will be mailed to the participant. This will include a pre-paid postage return envelope. The consent will be discussed in detail via telephone.

Once the consent is completed and returned, then the interview will be conducted via the phone. Consent will include a discussion of study rationale, procedures, measures, benefits, risks, and

alternatives to participation. The in person interviews will be conducted at Karabots and anticipate to last for up to an hour. See Appendix 5 for the interview guide.
Consent will include a discussion of study rationale, procedures, measures, benefits, risks, and alternatives to participation. The in-person interviews will be conducted at Karabots and anticipate to last for up to an hour. See Appendix 5 for the interview guide.

3.1.2 Study Treatment Phase (start of the study intervention)

Once recruited, newborns and their parent will be randomized into either the intervention or the control group. Children randomized to the early literacy promotion arm will receive developmentally appropriate books, information on the importance of early parent-child reading activity by pediatric clinicians, and weekly text message reminders concerning early literacy and daily reading activity at well child visits from one week to 6 months of age. Developmentally appropriate books will be selected for each well child visit prior to 6 months of age. Information on early literacy will be standardized and age-based and will be provided to parents by pediatric clinicians at well visits prior to 6 months of age. The weekly text message reminders will be initiated following enrollment, will be standardized, and will be scheduled according to parent preference in the morning, afternoon, or evening. The text message reminders will help remind parents to ensure that children in the intervention arm are exposed to parent-child reading activity in their first six months of life. Sample text messages are included in Appendix 5. In order to avoid any bias, parents of children in the control group will also receive weekly text messages focused about child safety instead of reading tips or advice. Beginning with the 6-month well child visit, children in this arm will receive the standard ROR Program as described in the standard literacy promotion group below.

Children randomized to the standard literacy promotion arm will receive developmentally appropriate books and information on the importance of parent-child reading activity by pediatric clinicians beginning with the 6-month well child visit and weekly text message reminders concerning child safety. This conforms to the ROR National Program recommendations and is considered standard of care at these 3 urban clinics. To prevent contamination in which pediatric clinicians inadvertently provide books and instruction on reading activity to control children prior to 6 months of age, a research assistant will ensure that books and reading instruction are not provided to children in this arm prior to 6 months of age. The weekly text message reminders will be initiated following enrollment, will be standardized according to age, and will be scheduled according to parent preference in the morning, afternoon, or evening.

Children in both study arms will be followed every 6 months until age 2. Parents will complete study measures consisting of demographic characteristics, postpartum depression symptoms, health literacy, and adverse childhood experiences at enrollment, and parents and children will complete measures of reading activity (Stim-Q), and child expressive and receptive language development (Preschool Language Scale-V) at 6, and 24 months of age. At 12, 18, and 24 months, measures of parental stress (PSI-Short Form, Appendix 9), parental depression (PHQ-9, Appendix 10) will be collected. Child social and emotional competencies will be collected at 18

and 24 months of age (ITSEA, Appendix 11). Information on reading activities and expressive and receptive language outcomes will be collected in concert with scheduled well child visits. Differences in reading activities, parental mental health, childs social/emotional competencies, and language outcomes will be assessed between groups using intention-to-treat analysis. The EHR will be reviewed for children in both arms to count the number of well child visits and examine their vaccination history.

Parents of children who are participating in the study will be informed of the results of their PLS testing in writing. Those whose children score less than 1.5 standard deviations below the mean will be informed that their children's language development is within the average range. Parents whose children who score 1.5 standard deviations or greater below the mean will be informed that their child is exhibiting delays in language development and will be referred for additional evaluations and/or services. In addition, the child's clinician will be informed of their result.

Responses to the question on the PHQ-9 will be checked to determine whether the caregiver has endorsed suicidal ideation. If they have endorsed any of the suicide questions, research staff will administer additional follow up questions and call the study licensed psychiatrist to determine course of action (see Appendix 13-Suicide Protocol). This procedure has been implemented successfully in other studies of parental depression. During the study visits, if a participant was to endorse suicidal ideations, the Appendix 13: 'Suicide Protocol' will be followed to maximize the safety of the participant. At any time, caregivers who endorse suicidal ideations will require immediate follow up with the licensed psychiatrist on call.

Up to 30 parents with infants less than 6 months of age with an equal mixture of high and low ACE's will be recruited to participate in interviews during the first year of the study. An interview guide will be utilized and include probes to assess perceptions, barriers, and promoters of reading at the parent, family, and environmental level. The interviews will be audiotaped, transcribed, and stored on a secure CHOP server. See appendix 5 for interview guide.

3.2 Allocation to Treatment Groups and Blinding

Children will be randomized to receive early literacy promotion or standard literacy promotion. Randomization sequences will be developed by the project biostatistician using computer-generated random numbers prior to study enrollment and will be placed in sealed opaque envelopes. The control group will not receive the early literacy promotion program, and will instead receive standard literacy promotion over the course of the study beginning at 6 months of age.

3.3 Study Duration, Enrollment and Number of Sites

3.3.1 Duration of Study Participation

The study duration per subject will be approximately 2 years following screening/consenting. For the sub-study, study duration will be for approximately 1 hour per participant with a 1 hour follow up focus group to triangulate findings and themes.

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

The study will be conducted at the Karabots Primary Care Center in Philadelphia, Pennsylvania, which has already implemented ROR as standard practice. This site has been individually recruited to participate (see PeRC letter of support) and has agreed to participate.

Recruitment will stop when approximately 240 subjects (120 dyads of parent and infant) are enrolled. For the qualitative component, recruitment for the semi-structured interviews will stop once 30 parents are enrolled or sooner if thematic saturation is achieved with fewer participants.

3.4 Study Population

3.4.1 Inclusion Criteria

1) English or Spanish speaking
2) Parents 15 years of age or older at the start of the study
3) Child born ≥ 35 weeks estimated gestational age
4) Child less than 4 weeks old at enrollment
5) Child with Medicaid Insurance
6) Phone with text messaging plan

3.4.2 Exclusion Criteria

1) Child born premature < 35 weeks EGA
2) Children with neurodevelopmental disabilities or congenital malformation at increased risk of language delays

3.4.3 Inclusion Criteria for Sub-study

1) Already enrolled in main study in the control group.
2) Parents enrolled in the control group with infants less than 6 months of age or not having 6 month well child visit.

3.4.4 Exclusion Criteria for Sub-study

1) Not enrolled in main study in the control group

2) Parents enrolled in the control group with infants older than 6 months or already having their 6 month well child visit.

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.

3) **STUDY PROCEDURES**

a. Screening/Consenting Visit and Study Visit 1

- Identify eligible newborns at the time of their first well child visit using the electronic health record (EHR)
- Recruit and consent eligible newborns and their parents at well child visits prior to 1 month of age
- Randomize newborns and their parents into intervention and control groups
- Collect baseline demographic, parent adversity, and parent mental health information
- Eligible parents for the semi-structured interviews will be identified after enrollment in the study. These parents will be notified regarding this separate component of the study, and those who are interested will receive additional informed consent to participate in the qualitative portion of the study. The qualitative interviews will be conducted during the first year of study with aims of 30 interviews or until thematic saturation is achieved.

b. Study Treatment Phase (enrollment until 4 month well-child visit)

- Conduct semi-structured interviews up to six months of age and follow up focus group
- Make reminder phone calls to all participants to schedule well visits
- Implement an EHR alert to remind clinicians of patients in intervention group at time of well visits at 1 month, 2 months, 4 months, and 6 months
- Provide developmentally appropriate books and reading script to clinicians to give to the members of the intervention group at enrollment, 1-month, 2-month and 4-month well visits
- Implement 24 weekly text message reminders about reading for intervention group
- Implement 24 weekly text message reminders about safety for control group

c. Follow-up Visits (at 6-, 12-, 18-, and 24- month well visits)

- Conduct semi-structured interviews up to six months of age

- Make reminder phone calls to all participants to schedule well visits
- Implement an EHR alert to remind clinicians of patients in both groups at time of well visits
- Schedule and complete study visits in conjunction with well visits at 6, 12, 18, and 24 months of age
    - Parents will complete measures of reading activity (Stim-Q) at each study visit.
    - Children will complete measure of child expressive and receptive language development (Preschool Language Scale-V) at 6- and 24-month visits.
    - At the 12-, 18-, and 24-month visits, parents will complete the PSI and PHQ-9 questionnaires.
    - At the18- and 24-month visits, parents will also complete the ITSEA about their child.

4) STUDY EVALUATIONS AND MEASUREMENTS

a. Screening and Monitoring Evaluations and Measurements

i. Parent Adversity (ACE)

The 9 ACE questions query adults as to their exposure to 9 different adverse childhood experiences (economic hardship, domestic violence, parent mental health, discrimination, parent substance abuse, divorce, parent death, parent incarceration, and neighborhood violence) and are contained in the 2011-12 National Survey of Children's Health, a nationally representative telephone survey.

ii. Parent Health Literacy (SAHL)

The Short Assessment of Health Literacy (SAHL) is a validated measure of health literacy for English- and Spanish-speaking populations.

iii. Parent Depressive Symptoms (EPDS)

The Edinburgh Postnatal Depression Scale (EPDS) is a validated 10-item scale for postpartum depression symptoms with scores ≥9 having a sensitivity of 97% and specificity of 43% for major or minor depression.

iv. Reading Activity (StimQ)

The StimQ is an office measure of cognitive stimulation at home available in Spanish and English, and the Read subscale of the StimQ contains questions on the frequency of parent-child reading activity and the number and variety of books at home.24 Psychometric analysis of the StimQ shows high internal consistency (Cronbach's Alpha=0.89) and test-retest reliability (r=0.84) and moderate correlation with the Bayley Scales of Infant Development (r=0.52, $p<0.001$).

We will also use a brief reading questionnaire (Appendix 12) about when participants began reading to their child and what influenced that decision.

v. Language Development (PLS)

The Preschool Language Scale-5th Edition (PLS) is a validated measure of expressive and receptive language function among children from birth through 7 years of age and is available in Spanish and English. The PLS has been standardized in over 1400 children nationally with a sensitivity of 0.83 and a specificity of 0.80 for the detection of language delay.

vi. Infant Toddler Social Emotional Assessment (ITSEA)

The ITSEA assesses for social or emotional problems and competencies in infants and toddlers and was designed to identify children with deficits or delays in these areas. It provides a comprehensive profile of problems and competencies with scores on 4 domains: 1) Externalizing 2) Internalizing 3) Dysregulation 4) Competence. Each domain is comprised of a number of subscales .The ITSEA also yields scores on three clusters that include atypical behaviors: Maladaptive, Social Relatedness, and Atypical.

vii. Patient Health Questionnaire – 9 (PHQ-9)

The Patient Health Questionnaire (PHQ) is a self-administered version of the PRIME-MD diagnostic instrument for common mental disorders. The PHQ-9 is the depression module, which scores each of the 9 DSM-IV criteria as "0" (not at all) to "3" (nearly every day). A PHQ-9 score ≥10 had a sensitivity of 88% and a specificity of 88% for major depression.

viii. Parenting Stress Index (PSI)

The PSI Short Form (PSI/SF) is a direct derivative of the Parenting Stress Index (PSI) full-length test. All 36 items on the Short Form are contained on the Long Form with identical wording and are written at a 5th-grade reading level, for parents of children 12 years and younger. The PSI/SF yields a Total Stress score from three scales: Parental Distress, Parent-Child Dysfunctional Interaction, and Difficult Child. Scores at or above the 85th percentile are considered high and Defensive Reponding scores at 10 or below are considered extremely low.

ix. Qualitative Measures

An interview guide with appropriate probes will be utilized to guide the semi-structured interviews. Areas that will be investigated include: understanding parent's perception of value in reading to their infant, factors that promote reading, and barriers that inhibit/limit reading. Elements of parent characteristics, family support and structure, and community factors will be explored through semi-structured interviews. As is typical in qualitative research, the order of questions and phrasing may change iteratively without changing content or risk. A purposive sample of parents as described previously in the section regarding the investigational plan will be selected to participate in the interviews. Interviews will be conducted with the goal to achieve

thematic saturation and elicit themes. The interviews will be recorded, transcribed, and stored on a secure CHOP server.

5) STATISTICAL CONSIDERATIONS

a. Primary Endpoint

The primary endpoint will be differences in PLS scores at 6 and 24 months of age.

b. Secondary Endpoints

Secondary endpoints will be the difference in StimQ scores at 6, 12, 18, and 24 months of age and the ITSEA scores at 18 and 24 months of age.

c. Statistical Methods

Summary statistics will be obtained, and differences between intervention and control groups will be assessed using intention-to-treat analysis. Cross-sectional differences in StimQ scores and PLS scores between intervention and control groups at the 6 and 24 month study visits and differences in ITSEA scores at 18 and 24 month study visits will be assessed using t-tests. To determine whether early literacy promotion is associated with greater language development, we will develop regression models using longitudinal data methods that adjust for correlation in PLS scores over time and for potential confounding by demographic characteristics. To explore whether early literacy promotion is associated with greater child socio-emotional development, we will develop regression models for scores at 18 and 24 months that adjust for potential confounding by demographic characteristics. To explore the impact of early literacy on healthcare utilization, the EHR will be reviewed to identify a subjects number of well visits and their vaccination history.

To determine whether parent adversity, health literacy, parenting stress,, and/or depression modify the effects of early literacy promotion on language development, we will develop similar regression models using longitudinal data methods, but we will also fit interaction terms between study group and ACE score (≥4), SAHL (high or low), PSI score, and EPDS score (>9) or PHQ-9 Score (>4). To determine if parent-child reading activity mediates the association of intervention group assignment and language development, we will use mediation analysis with separate models regressing group assignment on language development, parent-child reading activity on group assignment, and group assignment on language development adjusted for parent-child reading activity.

Assuming a power of 0.90, an alpha of 0.05, a 20% loss to follow-up over two years, and a clinically significant difference of 4 points or more on the expressive and receptive subscales of the PLS between groups, we estimate that we will need to recruit a total sample size of 120 eligible children (60 in each group) to participate in the study. All analyses will be conducted using Stata Statistical Software, version 13 (College Station, TX).

We will use NVIVO software to assist in data management for the semi-structured interviews. This software facilitates thematic coding, the assessment of inter-rater reliability, and correlation of themes with demographic variables. After detailed review of each transcript, we will develop a coding scheme and dictionary. We will use the constant comparative method in which newly collected data are compared with categories that have emerged from previously collected data. Through an iterative process, we will discuss the emerging themes as a team and revise the interview guide as needed to explore in depth themes arising from the data. If differences in coding arise, two members will discuss the data and negotiate to reach a consensus. If consensus cannot be reached a third member will decide the outcome. Once thematic saturation is reached, findings will be shared with participants at a follow up focus group after interviews have ben conducted.

7. SAFETY MANAGEMENT

7.1 Clinical Adverse Events

Clinical adverse events (AEs) will be monitored throughout the study. The main risks are disclosure of private health information (PHI) and study responses and discomfort with answering sensitive questions concerning childhood trauma or depressive symptoms.

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. We will query participants concerning any disclosures of PHI at each study visit. We will only query participants once concerning childhood trauma and depressive symptoms at the baseline visit.

8. STUDY ADMINISTRATION

8.1 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.

Unique identifiers will be created for each subject in the study. REDCap will be used to store the data. Since we are using REDCap, we will not need to maintain a Master List separate from the rest of the data. Participants' information will be stored in the REDCap database and configured

to export data without PHI. All de-identified records will be retained forever. Coded, de-identified data will be shared with the study sponsor.

Any paper copies of research instruments will be stored using the patient's ID code and will be kept in the department of General Pediatrics at The Children's Hospital of Philadelphia.

For the sub-study, a CHOP Sharedrive will be used to store all transcripts and digital recordings. Only study personal will have accesses to this server. All audio recordings will be transcribed ted by ADP a professional transcription service. They will not receive any personal health information and will be asked to remove all names while transcribing. The study team has an established business relationship in place with ADP. All audio recordings will be destroyed within three years of data analysis completion.

8.2 Confidentiality

All data and records generated during this study will be kept confidential in accordance with Institutional policies and HIPAA on subject privacy and that the Investigator and other site personnel will not use such data and records for any purpose other than conducting the study with the exception of mandatory reporting requirements for child maltreatment.

No identifiable data will be used for future study without first obtaining IRB approval. The research staff will obtain a data use agreement between the provider (the PI) of the data and any recipient researchers (including others at CHOP) before sharing a limited dataset (PHI limited to dates and zip codes).

8.3 Regulatory and Ethical Considerations

8.3.1 Data and Safety Monitoring Plan

Monitoring of adverse events, mainly disclosure of PHI from medical records and study assessment responses, will be ongoing during the intervention period until all data have been de-identified. Participants will be asked whether they know of any breaches of confidentiality at all contacts with subjects. All non-serious adverse events including disclosure of information will be reported to the CHOP IRB at the time of continuing review and to the funding agency annually. The PI will be responsible for overseeing the monitoring plan. Trained research assistants under the supervision of the Principal Investigator will conduct monitoring of data and safety twice annually.

8.3.2 Risk Assessment

There is minimal risk for harm to the participant in this study. Some information collected from the study participants on the study assessments is sensitive information and may cause the subjects discomfort, e.g. questions concerning childhood trauma or depressive symptoms. This

could include assessment of caregiver's suicidal ideations and a screening of caregiver's suicide risk in primary care flow. Also, question #9 on the PHQ-9 can indicate suicidal ideation or suicidal risk. The results of the screener and the PHQ-9 (Appendix 10) will be reviewed soon after completion (See Appendix 4). Dr. Marsha Gerdes, PhD, is a co-investigator and child-psychologist who has expertise in early child development and measurement. She will serve as the licensed psychologist to contact if screener is positive or suicide risk is high. The follow-up plan is laid out in Appendix 13. This risk is considered minimal and no more than what is normally associated with being in a physician's or mental health practitioner's office. Furthermore, families incur a risk of disclosure of private health information to individuals not connected with this study. This could occur through inadvertent disclosure of PHI by research staff. This risk will be minimized by using the study identifier on all study instruments and the research database as well as storing identifying information in a separate place than study information.

Unique identifiers will be created for each subject in the study. REDCap will be used to store the data. Since we are using REDCap, we will not need to maintain a Master List separate from the rest of the data. Participants' information will be stored in the REDCap database and configured to export data without PHI. All de-identified records will be retained forever. Coded, de-identified data will be shared with the study sponsor.

8.3.3 Potential Benefits of Trial Participation

Participants in the intervention may not benefit from the early literacy promotion intervention. Their children may be more likely than those in the control group to improve their language development but these benefits can not be guaranteed. Parents and their poor at-risk children may benefit from initiating parent-child reading activity earlier with the potential for improved language development.

Information from this study could be used to generate generalizable knowledge to reshape the ROR program and provide information for other early literacy campaigns such as Philadelphia's Read! By 4th and the Great Start Collaborative's Early to Read Campaign. If results from this study favor the early literacy promotion arm, then administrators of the ROR program and other local and national literacy campaigns can encourage the distribution of developmentally appropriate books and discussion of the importance of reading by parents beginning at 1 month of age. Nationally, pediatric clinicians may benefit by knowing evidence of whether early literacy promotion can impact language development. Locally, pediatric clinicians could benefit by having CHOP's ROR program expanded to include newborn infants. Information from this study can be used by policymakers and grant funders to increase funding support to expand the ROR program and other local and national literacy campaigns to newborn infants.

8.3.4 Risk-Benefit Assessment

The risks to participants are minimal and further minimized through protections. The benefits of parents receiving advice and materials through the support of the early literacy promotion

program outweigh the risks of participation. Therefore, the risk-benefit ratio is considered favorable.

8.4 Recruitment Strategy

We will screen all infants scheduled for a well or follow-up visit prior to 30 days of age at Karabots for possible eligibility. Those deemed to be potentially eligible will be approached in person during their clinic visit to obtain informed consent from their parents. We will also hang recruitment flyers in the hallways at Karabots giving information about the study and contact information for the study coordinator in case they are interested and we miss their names in the screening.

All parents that participate in the main study will be eligible for the qualitative component of the study. At time of enrollment into the main study, the qualitative component will also be discussed and separate informed consent obtained if participant is interested.

For families that have expressed interest in participating in the qualitative study, but fail to present for an interview (including rescheduling up to 2 times), we will offer to conduct the interview via telephone. Phone calls will take place on a secure line. These interviews will also be recorded and transcribed. Informed consent will be obtained for these participants prior to participation. Consent forms will be mailed to the participant. Consent will be discussed via the telephone with the participant. Once the consent form is mailed back and received, the interview will proceed via telephone.

8.5 Informed Consent/Assent and HIPAA Authorization

During the research staff visit after screening, written informed consent will be completed. Following the screening via review of the medical record, eligibility for study participation will be explained, either in person or via phone. 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. Parents who agree to participate will sign two copies of the informed consent form and be given one for their personal files. 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. Parents who choose to participate will be asked to sign the written informed consent documents in duplicate: one will be kept for study purposes and the other will be provided to the consenting parent.

For in-person qualitative interviews: Following recruitment and setting up a meeting, informed consent will be obtained on-site at the day of the interview. Research staff will discuss the study aims, procedures, risks, benefits, alternatives to participation and provide the potential subject the opportunity to ask questions about the study and its risks and benefits. If the participant consents, then the interview will be conducted immediately following their consent form being signed.

For qualitative interviews conducted via the phone: An informed consent discussion will be conducted over the phone. Research staff will discuss the study aims, procedures, risks, benefits, alternatives to participation and provide the potential subject the opportunity to ask questions about the study and its risks and benefits, allowing the participant to ask any questions. If the participant consents, they will mail the signed form back to the study staff (i.e. written consent will be obtained). The interview will then be conducted following the participants signed consent form being mailed and received by the study staff.

8.6 Payment to Subjects/Families

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

All participating parents will be paid up to $330 total for their participation in the main study. They will receive $50 at the point of enrollment/initial study visit. They will receive $40 for completion of the study visits at 6 months, $60 for the study visits at 12- and 18-months, and $120 for the visit at 24-months. All payments will be made in the form of pre-paid, CHOP-issued debit cards.

All parents, who participate in a semi-structured interview, will receive $40 for their participation in the interview. They will also receive $20 for their participation in the focus group in addition to SEPTA tokens if needed for their transportation. For parents who participate in phone interviews, they will receive the compensation in the mail directly following their interview.

8.6.2 Gifts

Parents participating in the intervention will receive tote bags at their enrollment and four books over the course of the first four months of the study, one at each well visit (enrollment within first week of life, 1 month, 2 month, and 4 months). All parents will receive a small gift to thank them for participating at the end of the final study visit.

9 PUBLICATION

We propose a multipronged dissemination strategy for this study that will have the goal of distributing study results to scientific audiences, lay audiences, policy audiences, and parents. If funded, we will work with the Strategy Team at Policylab at CHOP to implement this dissemination strategy. We will present findings from this study at the Pediatric Academic Societies annual meeting, where pediatric clinicians, early literacy experts, and Reach Out and Read advocates attend. We will also develop 4 peer-reviewed manuscripts for publication and target them to pediatric and child health journals in order to reach a clinical and scientific audience. One manuscript will report the overall results of the randomized controlled trial of early literacy promotion vs. standard literacy promotion. A second manuscript will report the results of the moderator analysis, which will attempt to determine if early literacy promotion is more beneficial in selected high-risk populations such as parents who experience childhood adversity or who have mental health conditions. A third manuscript will be prepared to report the results of the mediation analysis in which we will attempt to determine whether the effects of early literacy promotion and/or standard literacy promotion are mediated through parent-child reading activity and/or Reach Out and Read sessions at well visits. Study participants will not be identified in any publication stemming from this study. A fourth manuscript will discuss barriers and promoters to reading behaviors.

To reach lay and policy audiences with findings from this study, we will place a summary of the results of the study on the Policylab website (http://policylab.chop.edu/) and tweet the results to our Policylab twitter followers. This latter group is a diverse group of individuals from policy, advocacy, government, and clinical fields. We will also prepare an Evidence-to-Action (ETA) policy brief, which attempts to capture the policy implications of the study findings. ETA briefs, which are developed at Policylab, are mailed and/or emailed to policymakers and child health advocates on our distribution list.

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APPENDIX

See attached