Study Title: Enhancing Communication Between Children in EI and Their Depressed Mothers

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PROTOCOL TEMPLATE: INTERVENTIONAL STUDY

Complete Title: Enhancing Communication Between Children in EI and Their Depressed Mothers

Short Title: Using the LENA System in Early Intervention - b

Drug or Device Name(s): NA

FDA IND/IDE (if applicable): NA

Sponsor: University of North Carolina, Chapel Hill

Protocol Date: 10/12/2019

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Amendment 3 Date: NA

Amendment 4 Date: NA

Sponsor (IND or IDE holder, if applicable)
North Carolina Translational & Clinical Sciences Institute
Brinkhous-Bullitt Building, CB#7064
University of North Carolina at Chapel Hill
Chapel Hill, NC 25799-7064
USA

Linda Beeber, Ph.D., PMHCNS-BC
The University of North Carolina at Chapel Hill
School of Nursing
Carrington Hall, CB #7460
Chapel Hill, NC 27599-7460
Phone: 919-966-8148
email: beeber@email.unc.edu

PROTOCOL TITLE: Enhancing Communication Between Children in EI and Their Depressed Mothers

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Lead Investigator:

Linda Beeber, Ph.D., PMHCNS-BC
University of North Carolina at Chapel Hill

Protocol Version: 1.0

Version Date: October 12, 2019

I confirm that I have read this protocol and understand it.

Principal Investigator Name: Linda S. Beeber

Principal Investigator Signature: 

Date: 10/12/2019

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ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
EI	Early Intervention
LENA	Language Enhancement/Intervention System
PSOC	Parenting Sense of Competence
PHQ-9	Patient Health Questionnaire – 9
GAD-7	Generalized Anxiety Disorder – 7 item

PROTOCOL SYNOPSIS

Study Title	Enhancing Communication Between Children in EI and Their Depressed Mothers
Funder	North Carolina Translational and Clinical Sciences Institute, University of North Carolina at Chapel Hill
Clinical Phase	NA
Study Rationale	While maternal depressive symptoms can disrupt developmentally stimulating, child-centered speech, simple tools to assess and provide feedback to mothers can improve the child-centered speech and reciprocal language interactions that positively impact child outcomes. Although the LENA has been used in other studies and shown improvements in mothers' child-centered speech, the system has not been used with mothers showing depressive symptoms or in the EI context.
Study Objective(s)	Primary • To test the feasibility and initial efficacy of embedding a language pedometer, the Language ENhancement Assessment/Intervention system (LENA) into Early Intervention (EI) to teach mothers to increase child-centered speech and reciprocal communication.
Test Article(s) *(If Applicable)*	Mothers who will run the Language Enhancement Assessment/intervention system with their young children, and will receive initial feedback from researchers on LENA output and how to enhance the language in the home language environment. The intervention involves mothers independently running the LENA system, an audio recorder language pedometer that records adult speech centered on the child, child vocalizations, and parent-child reciprocal turn-taking conversations. Researchers will provide an initial feedback session, which will include reviewing the LENA visual output from the previous recording and how mothers can access the output on their own for future recordings. Mothers will independently use the LENA system and access the output on their own.
Study Design	The investigators will examine the efficacy of using LENA in a pre-/post intervention design, where mothers will run the LENA for 1 day a week for a total of 6 weeks. Outcome measures will be collected prior to the first LENA recording and again after the final recording.
Subject Population	Inclusion Criteria 1. Subjects age 18-99 years

key criteria for Inclusion and Exclusion:	2. Biological or adoptive mother of an infant (6 weeks – 18 months old) or toddler (19-32 months old) enrolled in EI at the time of recruitment; mothers must be the primary caretaker of the child 3. Able to give consent independently, and must have adequate capacity to participate in the LENA intervention as well as understand what they will be asked to do as participants. Exclusion Criteria 1. Currently pregnant by self-report 2. Child is completely deaf
Number Of Subjects	10
Study Duration	Each subject's participation will last approximately 2 months. The entire study is expected to last 12 months.
Study Phases Screening Study Treatment Follow-Up	(1) Screening: screening for eligibility, (2) Enrollment/Baseline: obtaining consent and conducting Time 1 outcome measures prior to intervention, (3) Intervention: study intervention using the LENA, and (4) Post-test/Analysis: Time 2 outcome measures after intervention and analysis
Efficacy Evaluations	Primary evaluation measure that will be used to assess the efficacy of the intervention is the LENA Adult Word Count.
Pharmacokinetic Evaluations	NA
Safety Evaluations	The MPIs will regularly monitor the study and data collection procedures and meet with the EI staff to review the protocols for safety and confidentiality. Drs. Beeber and Meltzer-Brody will constantly monitor mothers whose depressive symptoms worsen and will arrange for immediate assessment if needed.
Statistical And Analytic Plan	Due to the small sample size and the feasibility/exploratory nature of the research questions, analyses will be descriptive only (means, standard deviations and/or frequencies).
DATA AND SAFETY MONITORING PLAN	The safety plan is described above. For management of data quality, Dr. LaForett will work with Dr. Okoniewski, Ms. Salomon, and staff keying data to ensure data management activities (initial data cleaning, double keying, error checking and error corrections, and data validation) are conducted.

1 BACKGROUND AND RATIONALE

1.1 Introduction

Early Intervention (EI) services are provided to infants and toddlers with documented developmental delays in all 50 states and US territories. EI improves long-term infant-toddler adaptation and lowers the cost of care if parents use the services. However, depressive symptoms can reduce mothers' ability to provide the daily child development-promoting activities recommended by EI, increasing the child's risk for communication and behavioral problems. Indeed, repeated studies have shown that depressive symptoms reduce mothers' consistent use of developmentally sensitive, child-centered speech which, in turn, leads to negative child cognitive and behavioral outcomes.

1.2 Name and Description of Investigational Product or Intervention

The Language ENhancement Analysis (LENA; www.lenafoundation.org) system uses a non-invasive wearable sensor that (i) records language input and output, and (ii) provides visual feedback. When paired with simple tips for improving verbal input, it increases the quantity and quality of adult-child verbal interactions (Suskind et al., 2013). LENA is a validated tool for assessing adult and child speech and reciprocal interactions (Xu et al., 2009). The LENA system quantifies the number of words a child is exposed to, and the number of conversational turns between a child and adults over a 16-hour period (Gilkerson & Richardson, 2008). The LENA uses a shirt, vest or infant one-piece garment with an integrated audiotape device that records adult speech centered on the child, child vocalizations, and reciprocal turn-taking conversations between parent and child. Environmental noise (e.g., TV, non-caretaker speech) also can be recorded and analyzed in segments by LENA software. The quantified "language environment" is presented in a series of graphs which can be shown to parents to assist with goal setting. A "biofeedback" intervention model combines the visual data provided by LENA with customized "talking tips" for increasing adult word count and conversational turn taking (http://www.providencetalks.org/wp-content/uploads/2015/09/Binder1.pdf), which in turn results in improved reciprocal communication.

1.3 Non-Clinical and Clinical Study Findings

This LENA intervention model showed success in increasing adult language production in parents of typically developing children (Suskind et al., 2013). In addition, LENA has been used successfully to document exposure to adult language in parent-child dyads in low-income families (Weisleder & Fernald, 2013), children with hearing loss (Caskey & Vohr, 2013), newborns in NICUs (Caskey et al., 2014), and in children with autism (Irvin et al., 2013; Yoder et al., 2013), and Down syndrome (Thiemann-Bourque et al., 2014). However, none of these studies explicitly explored the language environments of children with disabilities and mothers with depression, or "dually vulnerable" dyads, and no studies have addressed the use of LENA as an embedded tool within existing EI systems.

There are no known or expected risks to using the LENA system.

1.4 Relevant Literature and Data

Previous research showed that over one-third of mothers of children with disabilities have significant levels of depressive symptoms, a rate higher than the population at large. Infants and toddlers of

depressed mothers have been shown to receive fewer intensive services and have been shown to interfere with uptake of EI services through impaired mother-child interactions. A preliminary study by the investigators found that over a third of mothers in a large North Carolina county had severe depressive symptoms and depression histories. Fortunately, investigators also found that when depressed mothers were provided with concrete, attainable skills for improving interactions with their child, the impact of depression on both mother and child was substantially reduced. Focusing on a depressed mother's child-centered speech and reciprocal communication also improves outcomes, even when the child is cognitively compromised. However, none of these specialized services are part of EI best practices. Thus, EI is an ideal setting in which to integrate screening, referral, and targeted skills for depressed mothers in order to improve parent-child interactions and ultimately, child outcomes.

For the measures used to evaluate the efficacy of the LENA intervention, all have established reliability and validity: LENA adult word count, turn-taking, and child vocalizations (Xu, 2009); Parenting Sense of Competence (PSOC: Gilmore & Cuskelly, 2008); Patient Health Questionnaire – 9 (PHQ-9: Kronenke et al., 2001); Generalized Anxiety Disorder – 7 items (GAD-7: Spitzer et al., 2006).

2. STUDY OBJECTIVE

This project seeks to test the efficacy of this type of maternal-child focused intervention, using the LENA intervention embedded in EI to help mothers enhance their child-centered speech and reciprocal communication.

2.1 Primary Objective

The primary objective of the study is to test the feasibility and initial efficacy of embedding a language pedometer, the Language ENhancement Assessment/Intervention system (LENA) into Early Intervention (EI) to teach mothers to increase child-centered speech and reciprocal communication.

2.2 Secondary Objective - NA

3. INVESTIGATIONAL PLAN (brief overview)

3.1 Study Design

Type of design: Single group assignment, pre-/post-intervention

Provide brief overview of the study phases:

- Screening: screening for eligibility
- Enrollment/Baseline: obtaining consent and conducting Time 1 outcome measures prior to intervention
- Intervention: study intervention using the LENA
- Post-test/Analysis: Time 2 outcome measures after intervention and analysis

3.2 Allocation to Treatment Groups and Blinding (if applicable): NA

3.3 **Study Duration, Enrollment and Number of Subjects** 10 subjects will participate in the study. Each subject's participation will last approximately 2 months. The entire study is expected to last 12 months.

3.4 Study Population

Inclusion Criteria

- Subjects age 18-99 years
- Biological or adoptive mother of an infant (6 weeks – 18 months old) or toddler (19-32 months old) enrolled in EI at the time of recruitment; mothers must be the primary caretaker of the child
- Able to give consent independently, and must have adequate capacity to participate in the LENA intervention as well as understand what they will be asked to do as participants.

Exclusion Criteria

- Currently pregnant by self-report
- Child is completely deaf

4. STUDY PROCEDURES (what will be done)

4.1 Screening procedures

Interest letters describing the study will be mailed from our Part C research partner to mothers in April -June 2018. Interested mothers will contact the research team by phone or email to schedule a time to screen them for eligibility for the study. Screenings will be done via phone by a research team member who will administer the PHQ-9 and collect demographic information.

4.2 Enrollment/Baseline Visit procedures

For eligible mothers, researchers will schedule a home visit to go over enrollment procedures (i.e., complete consent forms). Enrolled mothers and their child who was the target for the study will complete the pre-test (Time 1) measures: the PHQ-9, the Parenting Sense of Competence, and the GAD-7. At this visit, mothers will be given written instructions and a video tutorial on how use the LENA system. The research team will leave the LENA recorder, clothing, and pre-stamped/addressed envelopes for the mother to mail the LENA recorder to the study team after the first recording was completed.

4.3 Intervention/Treatment procedures (by visits)

Mothers will run the Language Enhancement Assessment/intervention system with their young child for the first time for one day up to 16 hours and will mail the recorder back to the research team. Researchers will provide an initial feedback session, which will include reviewing the LENA visual output from the previous recording and how mothers can access the output on their own for future recordings. Mothers will independently use the LENA system and access the output on their own for 5 additional recordings over 5 weeks, again mailing each recorder back to the team after the receiving it again from the research team once the recording is uploaded to the LENA system.

4.4 Post-test/Analysis procedures (by visits)

Once the final recording is returned, researchers will schedule a home visit to complete the post-test (Time 2) measures: the PHQ-9, the Parenting Sense of Competence, and the GAD-7.

Researchers will conduct descriptive analyses including means, standard deviation and/or frequencies.

4.5 Unscheduled visits NA

4.6 Concomitant Medication documentation NA

4.7 Rescue medication administration (if applicable) NA

4.8 Subject Completion/ Withdrawal procedures

Once recordings were completed an exit interview was conducted. Upon completion of this interview incentives were mailed to participants and subject participation was considered complete.

4.9 **Screen failure procedures**

We did not have any screen failures.

5. STUDY EVALUATIONS AND MEASUREMENTS (how measurements will be made)

5.1 Efficacy Evaluation (if applicable)

The following measures will be used to evaluate feasibility and efficacy of the LENA intervention; LENA data will be derived from the LENA audio recording. All other measures are collected using maternal self-report.

Primary:

- Change in LENA Adult Word Count after 6 weeks: The LENA system, which records adult-child vocalizations, measures the number of the target adult's (e.g., parent's) child-directed words (child-directed speech). The total possible range is 0-n, where higher scores indicate an increased number of child-directed words spoken by the target adult and higher degrees of a language-rich environment. Lower scores indicate fewer words spoken by the target adult and represent an environment that is not language-rich.

Secondary:

- Change in Parenting Sense of Competence Scale after 6 weeks: The Parenting Sense of Competence Scale is a 17-item measure assessing parental competence. Each item is rated on a 6-point Likert scale anchored by 1=Strongly Disagree and 6=Strongly Agree. The Efficacy subscale measures feelings of efficacy as a parent. It has 7 questions (1, 6, 7, 10, 11, 13, 15), producing a range of 6-42. Higher scores indicate greater self-efficacy. Lower scores mean more impairment.

- Change in the Patient Health Questionnaire – 9 after 6 weeks: The PHQ-9 is a depression scale used to assess brief depression severity by rating symptoms and functional impairment experienced in the last two weeks. The questionnaire contains a total of 9 questions, and each question is scored on a range from 0-3. The minimum value "0" represents not at all, "1" several days, "2" indicates more than half the days, and the maximum value "3" stands for nearly every day. The total possible range is 0-27, with higher scores indicating more depressive symptoms. The total number of each 0, 1, 2, 3 is added and multiplied by its value (0=0, 1=1, etc.) to produce a total score generated from the subtotal sum. The PHQ-9 total score is interpreted as follows: 0-4 represents minimal depression, 5-9 as mild depression, 10-14 as moderate depression, 15-19 moderately severe depression, and 20-27 severe depression.
- Change in LENA Mother/Child Turn Taking after 6 weeks: The LENA system, which records adult-child vocalizations, measures the number of conversational turns between the target adult (e.g., parent) and child. The total possible range is 0-n, where higher scores indicate and increased number of turns (back-and-forth, or "reciprocal" language exchanges) between the adult and child, reflecting higher degrees of a language-rich environment. Lower scores indicate fewer conversational turns between the adult and child, and represent an environment that is not language-rich.
- Change in LENA Child Vocalization after 6 weeks: The LENA system, which records adult-child vocalizations, measures the number of vocalizations of the target child. The total possible range is 0-n, where higher scores indicate an increased number of vocalizations from the child, reflecting higher levels of language development. Lower scores indicate fewer vocalizations from the child, and represent lower levels of language development.
- Change in GAD-7 after 6 weeks: The Generalized Anxiety Disorder 7-item (GAD-7) is a self-report screening of anxiety symptoms examining frequency of the specific behaviors within the last two weeks (e.g., not at all - nearly every day). A total score is calculated and compared to pre-determined cutoffs to help guide professionals in next steps for evaluation and treatment.

5.2 Pharmacokinetic Evaluation (if applicable) NA

5.3 Safety Evaluations

The Co-PIs will review any questionable situation immediately; the research team will review all data collections weekly.

The MPIs will regularly monitor the study and data collection procedures and meet with the EI staff to review the protocols for safety and confidentiality. Drs. Beeber and Meltzer-Brody will constantly monitor mothers whose depressive symptoms worsen and will arrange for immediate assessment if needed.

6. STATISTICAL CONSIDERATION

Researchers will conduct descriptive analyses including means, standard deviation and/or frequencies. Our sample size of 8 mothers does not allow us to test pre/post changes. Nonetheless, this descriptive information will give us an initial sense of the feasibility and efficacy of the LENA intervention.

6.1 Primary Endpoint

The primary endpoint is 6 weeks after the LENA intervention.

6.2 Secondary Endpoint - NA

6.3 Statistical Methods

Researchers will conduct descriptive analyses including means, standard deviation and/or frequencies. Our sample size of 8 mothers does not allow us to test pre/post changes. Nonetheless, this descriptive information will give us an initial sense of the feasibility and efficacy of the LENA intervention.

6.4 Sample Size and Power

The sample size of 10 mothers is adequate to examine initial feasibility.

6.5 Interim Analysis - NA

7. STUDY INTERVENTION (drug, device or other intervention details)

Mothers will run the Language Enhancement Assessment/intervention system with their young child for the first time for one day up to 16 hours and will mail the recorder back to the research team. Researchers will provide an initial feedback session, which will include reviewing the LENA visual output from the previous recording and how mothers can access the output on their own for future recordings. Mothers will independently use the LENA system and access the output on their own for 5 additional recordings over 5 weeks, again mailing each recorder back to the team after the receiving it again from the research team once the recording is uploaded to the LENA system.

8. STUDY INTERVENTION ADMINISTRATION(if applicable)

NA

9. SAFETY MANAGEMENT

Mothers will be observed for fatigue and encouraged to tell the research team that they are too tired to continue. In such cases, the data collection session will be terminated and a follow-up session scheduled. Our preliminary and ongoing studies have shown that some mothers may not read well and become fatigued. Questionnaires are written clearly and simply and have been tested with mothers with limited literacy. Questionnaires will be read orally to all mothers if they wish. Visual aides in the form of printed response sets will be given to mothers so that they can point to the desired responses.

Plans to ensure necessary intervention in emotional distress: Research staff will follow a protocol for emergency situations and the project will adhere to the state legal statutes governing mandated reporting of suspected child abuse. If, during any contact with a project staff member, a mother expresses suicidal ideation, or is so immobilized by symptoms that she or her child are in danger, or is in danger because of domestic violence, the research staff member will assess the mother, contact the PI's and Project Coordinator, and, if with the mother, will remain with her until a safe resolution has been reached, i.e., immediate referral to a community resource and/or involvement of supporters who can continue to ascertain the safety of the mother and infant/toddler after the team member leaves the premises.

The decision about which resources to refer the mother will be made in consultation with the PI's and Co-Investigator Meltzer-Brody, a psychiatrist specializing in women's mood disorders and with the mother's permission, the CDSA Service Coordinator. The project will maintain a log of all incidents requiring emergency, immediate response, or referral, and will report exceptional incidents to the IRB as appropriate. Dr. Beeber, Dr. Wheeler, Dr. LaForett, the Project Coordinator (Salomon) and Dr. Meltzer-Brody are licensed mental health professionals familiar with depressive symptoms and emergency situations. The protocol will ensure that one or more of these research team members is on call for such situations. At the last contact with the study, mothers will receive a mental health resource referral list and with their permission, the CDSA Service Coordinator will be consulted as well to assure continuity. A review of all mothers actively in the project will be conducted in weekly research team meetings with the PI's and when needed, Dr. Meltzer-Brody.

10. DATA COLLECTION AND MANAGMENT

Mothers will be told that all data will be separated from the consent forms and identified by a number and that only the research team will have access to the names and numbers. The identity of participants will not be divulged to anyone except in the instance that the mother cannot be located through the contacts she has provided. In that instance, Durham CDSA will be contacted for information about the mother's current location and mothers will give the project written permission for this exception as part of their study consent. Permission to Contact forms will be kept in a locked file in a locked office at the Durham CDSA program until retrieved by a research team member. All study data will be kept in a locked office and a locked file at the FPG office. Data management procedures will include initial data cleaning, double keying, error checking and error corrections, and data validation prior to analysis. Data will be reported in aggregate form only, without identifying information by individual or site. All personnel will be trained to maintain security and confidentiality of the data. The mothers will be apprised of these precautions.

11. RECRUITMENT STRATEGY

Interest letters describing the study will be mailed from our Part C research partner to mothers in April -June 2018. Interested mothers will contact the research team by phone or email to schedule a time to screen them for eligibility for the study. Screenings will be done via phone by a research team member who will administer the PHQ-9 and collect demographic information. Researchers will give mothers opportunities to ask questions about the nature of their participation. If mothers speak Spanish,

materials will be available in Spanish and the screening process will be completed by a research team member who is bilingual in English and Spanish.

Although our original inclusion criteria included individuals with a PHQ-9 score greater than 8, we were not able to include recruit enough mothers who met this criterion, so we dropped it from our eligibility criteria.

12. CONSENT PROCESS

For eligible mothers, researchers will schedule a home visit to go over enrollment procedures (i.e., complete consent forms). Researchers will give mothers opportunities to ask questions about the nature of their participation. If mothers speak Spanish, materials will be available in Spanish and the consent process will be completed by a research team member who is bilingual in English and Spanish.

13. PLANS FOR PUBLICATION

We have two papers in progress we will submit for publication.

14. REFERENCES

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15 APPENDIX

Nothing to report.