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THE JPB RESEARCH NETWORK ON TOXIC STRESS
A Project of the Center on the Developing Child HARVARD UNIVERSITY

Expanding the Testing of Novel Measures of Risk and Resilience in Pediatric Primary Care
Health's Early Roots and Origins (HERO) Study

Request for Applications

Section 1. Overview

Background
The purpose of this Request for Applications (RFA) is to solicit interest from HealthySteps practices in collaborating with The JPB Research Network on Toxic Stress, an initiative of the Center on the Developing Child at Harvard University (HCDC). Given HealthySteps' focus on improving the health and well-being of babies and toddlers, promoting school-readiness, and partnering with caregivers—and its robust reach—the HealthySteps sites are primed to serve as ideal partners for this phase of work.

The JPB Research Network on Toxic Stress is focused on building new measurement capacity that will empower pediatricians and parents to better understand, quantify, and mitigate the effects of significant adversity on the health and development of young children. To accomplish this, the Network and its partners (including pediatric practices and community leaders) have been developing a more robust set of metrics for the early childhood ecosystem that will make it possible to:

- enhance screening for individual differences in sensitivity to context through biological measures of stress activation and behavioral measures of the building blocks of resilience;
- strengthen the ability to make targeted referrals to well-matched services (when indicated), as well as convey credible reassurance for parents of children who are doing well, guided by direct assessments of child development and biological indicators of risk beginning early in infancy; and
- augment the capacity to measure variation in short-term intervention effects to inform ongoing, individualized management and sustainable payment for effective services.

The JPB Network has been in operation since 2015 and has guided the selection and pilot testing of candidate measures designed for implementation in primary care practice. The current battery consists of three categories of measures:

- Child biological metrics *(e.g., inflammation, stress hormones, oxidative stress)*
- Child behavioral metrics *(e.g., executive function)*
- Social and behavioral context metrics *(e.g., family structure and assets, neighborhood risk factors and resources)*

Following large-scale testing to generate normative values, the JPB battery will make it possible to identify the effects of adversity in children as young as 4 months of age as well as factors that promote resilience throughout the early childhood period. When deployed responsibly, it will strengthen the capacity of primary care providers to partner collaboratively with parents to engage in preventive services before overt problems emerge; more effectively measure short-term impacts of interventions on learning, behavior, social-emotional development, and health; and facilitate continuous learning and iteration of services.

An authentic partnership and exploration of advances in early childhood health among HealthySteps sites and the JPB Network will enhance future early detection and linkage to supportive intervention efforts for families and their children. As we continue to advocate for ongoing surveillance and screening in the context of all that is known of the child and family, expanding awareness of a broader

set of measures related to risk and resilience will maximize our capacity to ensure responsive, appropriate, and beneficial referral and linkage activities.

Current Opportunity

We are seeking 2 – 5 pediatric practices to join an existing cohort of clinics assessing the implementation of measures in the context of well-child visits. Initial field testing of the JPB candidate measures was conducted by four distinct pediatric practices in New York, Texas, New Mexico, and Massachusetts connected to HCDC's Pediatric Innovation Initiative. As the JPB Network looks ahead to further scaling and, ultimately, systemic adoption of this measurement battery, there is a clear need to: (1) assess the implementation of the measures in a larger, diverse network of pediatric practices across the country (the focus of Phase 3 below); and (2) explore opportunities for primary care providers to engage with community-based, early childhood systems in their adoption and utilization of information from the measures (a key component of Phases 3-5 described below).

Project Trajectory

Our projected pathway to completion of the measurement development process and ultimate implementation at scale is summarized in the following 5-phase framework:

Phase 1: Discovery process to identify core scientific concepts, promising biological measures of stress activation, and key behavioral measures of resilience in young children to inform a deeper understanding of the origins of disparities in early learning, social-emotional development, and lifelong health. **[COMPLETED]**

Phase 2: Feasibility testing of candidate measures in a small cohort of pediatric primary care practices to learn about practical collection challenges and assess acceptability by both clinicians and parents in community settings. **[COMPLETED]**

Phase 3: Establish normative values to enable enhanced screening, **explore new candidate measures** to facilitate continuing refinement of the battery guided by advances in science, **test the utility of the battery as a measure of intervention effects**, and **lay the foundation for the implementation** of measures of stress activation in pediatric primary care. **[IN PROGRESS]**

Phase 4: Broader implementation with identified children and parents/caregivers in a controlled network of collaborating sites across a diversity of communities to learn more about benefits, pitfalls, and ethical challenges and continue to build a shared understanding of the value of the new measures—for screening, referral, measuring intervention effects, and securing payment for effective services.

Phase 5: Widespread adoption of new measurement capacity to generate greater impacts on early learning, social-emotional development, school readiness, and lifelong health at a population level.

Section 2. Participation

Project Objectives

This RFA is intended to solicit interest from HealthySteps sites to: (1) partner with HCDC and the JPB Network to establish normative values for a novel measurement battery in pediatric primary care; (2) learn more about how this information can help pediatricians and parents work together to address questions about stress and resilience in young children; (3) explore how enhanced measurement capacity can strengthen the role of pediatric primary care within community-based systems of early childhood services and supports; and (4) expand opportunities to promote ongoing communication and shared learning among participating clinic sites regarding both the benefits and the prevention of potential misuse of new measures of risk and resilience in young children.

Indices of excessive stress activation will be assessed through simple, non-invasive collections of biological samples, including saliva, a cheek swab for buccal epithelial cells, and a small (half the diameter of a pencil eraser) root-end hair sample, as well as a brief behavioral measure of executive function—all collectable during a pediatric office visit. Blood measures can also be examined if already being collected for clinical purposes, but they will not be mandatory. In addition to generating normative values for the biological and behavioral measures, other objectives of the ongoing field study of the battery are to evaluate: (1) the acceptability to parents of the collection of these biological samples and the analyses they enable; (2) the feasibility of biological and behavioral data collection during pediatric well-child visits; and (3) the range of variation we will find among key biological and behavioral indicators across a diversity of populations. We are also assessing the nature and magnitude of stressors and protective factors, both socioemotional and economic, that children and families are experiencing to inform the sensitivity and specificity of the measures.

Participation in HERO Phase 3 on behalf of the HealthySteps site will:

1. inform an important national dialogue about the implications and systemic considerations associated with expanding provider access to novel measures of child and family risk and resilience;
2. include a short series of virtual training modules provided by the study coordination team (based at HCDC and at the University of Minnesota) on protocol implementation, data collection, and acquiring local Institutional Review Board approval;
3. consist of monthly calls with the study coordination team and quarterly calls with the cohort of Phase 3 pediatric sites over the course of the project to share qualitative feedback and synthesize learning about successes and challenges; and
4. result in the collection, storage, and shipment of biological samples and tablet-based administration of a brief executive function task (for children age 2.5 and older) and social context questionnaire for approximately 300 children ages 4 months – 5 years (or ages 4 months – 3 years if your HealthySteps site only sees children until age 3) during their regular well-child visit.

Project Activities

Training and Pre-Implementation Planning
• Begin the contracting process with HCDC and other organizations affiliated with the study • Coordinate staff training on protocol and data collection procedures; training will be delivered by the study coordination team through a short series of virtual training modules and made available through an online training platform • Collaborate with the study coordination team to support practice personnel in navigating local IRB approval processes and establishing participant recruitment strategies • Establish a research team from the practice that will be responsible for study coordination and data collection, as outlined below

Implementation
• Work closely with the study coordination team to ensure study progress • Participate in regular calls with the study coordination team over the course of the implementation phase to share successes and challenges • Conduct the following in conjunction with well-child visits: recruit families and obtain informed consent; collect non-invasive samples of saliva, cheek swabs, and several strands of hair; coordinate blood sample collection (only if ordered for clinical purposes); administer the (tablet-based) executive function task for children ages 2.5 and older; administer the social context questionnaire with the parent/caregiver; and store and ship biological samples.

Eligibility

- Partnering pediatric practices must have the ability to fulfill these basic criteria:
    - participate in an informational interview following application review and prior to formal acceptance to the study;
    - establish study personnel from the practice who will be responsible for study coordination and data collection;
        - *A percentage of effort for this personnel will be supported by HCDC (see information regarding funding below).*
    - maintain clear and consistent communication with study coordinators during onboarding and study enrollment periods; and
    - recruit approximately 300 children ages 4 months – 5 years, balanced across age and sex within the regular well-child visit schedule.
- Preference may be given to pediatric practices that are able to fulfill these preferred criteria:
    - have experience conducting IRB-approved research, minimally within the organization and preferably amongst study team members;
    - serve a community that represents a diverse patient population that contributes to meeting the study goals of a nationally representative sample of 6,000 participants;
    - form a demographically and professionally diverse study team; and
    - include a proficient Spanish speaker on the study team who would be able to enroll Spanish-speaking participants in the study.

Other Relevant Details

- The target completion date for the project activities is December 2024, with the potential to extend through 2025 if necessary.
- Study implementation needs, including biological sample collection supplies, storage and/or shipping costs, an iPad for conducting the behavioral measure and social questionnaire, and a percentage of personnel effort will be supported at the practice level with funding directly from HCDC.
- **If you are interested in learning more about this opportunity, we strongly encourage you to attend the upcoming HealthySteps office hours on Thursday, March 16 from 12:00 – 1:00pm ET. Both the HealthySteps National Director as well as members of the study coordination team will be available to address questions at this time. If you would like to attend these office hours, please register here.**

Section 3. Application

1) Name of pediatric practice/site	2) Site contact name	3) Site contact email

4) Please include the following information about the site's patient population:
- basic demographic characteristics (including race, ethnicity) of the population served by the practice
- size of the pediatric population between 4 months and 5 years of age
    - Please note whether you plan to enroll all infants and toddlers in the practice (Tier 1) or limit it to Tiers 2 and 3.
    - Please note whether you plan to include children between 3 years and 5 years of age in study enrollment at your clinic.
- approximate number of well-child visits annually
- percent of the population who are Medicaid eligible
- any established programs and/or interventions in addition to HealthySteps that are regularly implemented by the practice and the approximate percentage of children receiving them

5) Please indicate the method by which you plan to identify personnel to support this study.
- Will existing staff be deployed on this study? What protected time will they have for this study, and how will they be supported in preserving that time?
- Will you need to hire new personnel to support the study? What is your projected timeline for making these hires?
- What experience do identified team members have with research in pediatric settings?
- How will responsibilities (study coordination, recruitment/consent, sample collection, and shipping) be divided amongst study team members?
- Study materials are available in English and Spanish; however, Spanish-speaking participants must be enrolled (and have MEFS administered) by a study team member who is fluent in Spanish. Does your site intend to enroll Spanish-speaking participants in the study? How might this decision impact your recruitment?

6) Facilities:
- Does your site have access to a locked research storage freezer on site? If so, at what temperature?
- Does your site have access to a biobank within 15 minutes of your practice? (Please see here for a list of biobanks and/or ask your colleagues: https://specimencentral.com/biobank-directory/#North%20American%20Biobanks.) If so, would you plan to use the biobank for storage of and to coordinate shipment of study samples?
- Does your site have access to additional space for administering the behavioral measure and/or social context questionnaire as necessary (e.g., additional exam rooms, conference rooms, etc.)?

7) Recognizing that the public health situation continues to impact healthcare practices worldwide, please share how your site is currently handling:
- telehealth vs. in-person well-child visits
- clinic appointment flow
- use of spaces (e.g., waiting rooms, exam rooms)

8). Please include a brief description of any previous research or data collection experience that your practice has successfully completed:

Please submit applications and all required materials to Katie Sherman (katie_sherman@harvard.edu) with the subject line: **RFA: Expanding the Testing of Novel Measures of Risk and Resilience in Pediatric Primary Care.** Applications will be reviewed on a rolling basis by HCDC and the HealthySteps National Office on the 1st of each month, until all openings are filled. Selected candidates will be notified by mid-month.