

Protocol Title:

HEARTPrep: A Virtually-delivered Psychosocial Intervention for Mothers Expecting a Baby With Congenital Heart Disease

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Note:

Aim 1 does NOT meet NIH's definition of a clinical trial. While it does involve human participants (criteria 1; YES) who are prospectively assigned to an intervention (criteria 2; YES), the study is NOT designed to evaluate the effect of the intervention on the participants (criteria 3; NO) nor to evaluate a health-related biomedical or behavioral outcome (criteria 4; NO).

Aim 2 does meet NIH's definition of a clinical trial. It involves human participants (criteria 1; YES) who are prospectively assigned to an intervention (criteria 2; YES), and the study is designed to evaluate the effect of the intervention on the participants (criteria 3; YES) and the effect being evaluated is a health-related biomedical or behavioral outcome (criteria 4; YES).

SPECIFIC AIMS

Congenital heart disease (CHD) is the most common birth defect (~1% of births),¹ frequently requiring cardiac surgeries, long hospitalizations, and intensive medical management. CHD affects all racial, ethnic, and socioeconomic groups,² yet **underserved populations (e.g., low-income Black and Hispanic patients) are disproportionately affected by disease-related morbidities**. They are more likely to be delivered preterm, to be readmitted to the hospital after surgery, to exhibit developmental delays, and ultimately, to die from CHD.³⁻⁷

CHD is increasingly diagnosed prenatally across racial/ethnic groups.⁸ While prenatal diagnosis can be beneficial for the infant in that it facilitates medical care immediately following birth,^{9,10} mothers describe their prenatal experiences as highly stressful/traumatic.^{11,12} **Maternal stress during pregnancy exerts a powerful influence on birth outcomes and developmental trajectories, particularly for children in underserved populations.**¹³⁻¹⁵ Prenatal diagnosis of a birth defect, such as CHD, adds substantial stress/trauma for mothers during a critical time period, at a level of severity known to impact child outcomes.¹⁶⁻¹⁸ Maternal stress has been shown to influence in-utero brain development and neurodevelopmental outcomes in CHD.¹⁹⁻²² However, fetal cardiology has focused mostly on evaluation of the fetal heart and informational support for decision making.⁹ **Targeted efforts to mitigate impacts of maternal stress for this highly vulnerable population are lacking.**

Our team recently designed HEARTPrep, an innovative, virtually-delivered psychosocial intervention for mothers expecting a baby with CHD. HEARTPrep will be delivered in English and Spanish through the Nemours App, a state-of-the-art tool for telehealth, education, and communication with clinicians. HEARTPrep was designed in partnership with parents of children with CHD from diverse backgrounds and multidisciplinary clinicians, and in accordance with the *ORBIT Model for Behavioral Treatment Development*, a systematic framework for developing behavioral interventions through rigorous *Phase I* and *Phase II* behavioral research.²³ In our preliminary work (*ORBIT Phase Ia: Define*),²⁴ parents identified four outcomes that need to be addressed during the prenatal period to promote long-term maternal/family wellbeing: emotional distress (↓), social isolation (↓), parenting self-efficacy (↑), and hope (↑). Parents and clinicians then identified intervention elements targeting each outcome, structured into three distinct HEARTPrep modules (*Adjusting, Connecting, Preparing*).

The proposed study will evaluate whether HEARTPrep improves maternal/family outcomes following prenatal diagnosis of CHD. We've assembled a team of experts in family-based psychosocial intervention and patient-centered outcomes research to refine HEARTPrep based on user feedback (*ORBIT Phase Ib: Refine*) and determine whether HEARTPrep produces clinically significant improvements (*Phase IIa: Proof-of-Concept*).

Aim 1: Refine HEARTPrep and evaluate initial feasibility, usability, and acceptability. Think Aloud testing²⁵ with 15-20 mothers expecting a baby with CHD will inform iterative improvements to HEARTPrep. The intervention will be beta tested with 40 additional mothers as it is being iteratively refined to evaluate initial feasibility, usability, and acceptability.

H1: Mothers will perceive the refined HEARTPrep intervention to be feasible, usable, and acceptable.

Aim 2: Determine whether HEARTPrep modules produce clinically significant improvements on outcomes in mothers expecting a baby with CHD (Proof-of-Concept). 40 mothers expecting a baby with CHD will receive HEARTPrep and will complete weekly assessment of outcomes before, during and following intervention.

H2: Mothers will demonstrate reduced distress and social isolation and increased parenting self-efficacy and hope (measured by PROMIS) after completing respective HEARTPrep modules targeting these outcomes.

Impact: HEARTPrep has the potential to improve the emotional wellbeing of mothers expecting a baby with CHD, thereby altering developmental trajectories for this large population of children. This model can then be adapted for other birth defects (3% of all births), given commonalities in maternal stress reactions,²⁶⁻²⁷ broadly addressing the disproportionate burden of disease-related morbidities in underserved populations.²⁸

A. SIGNIFICANCE

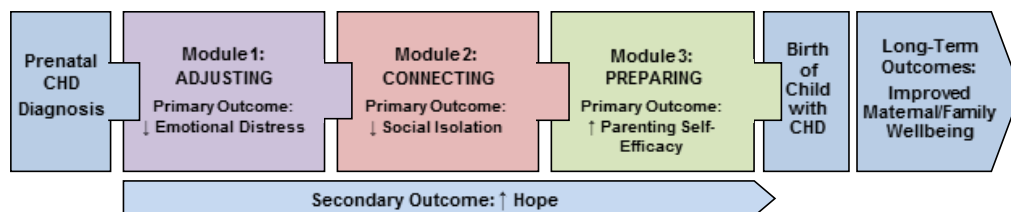
A.1. BACKGROUND. Congenital heart disease (CHD) is the most common birth defect, affecting nearly 1% of births in the United States, and is a leading cause of birth defect-associated infant illness and death.¹ One in four infants born with CHD require cardiac surgery in the first weeks or months of life, necessitating intensive care, long hospitalizations, and physical separation from parents during a critical period for parent-infant bonding and infant development. Infants with CHD not requiring early cardiac surgery are often subjected to intensive medical management and monitoring to determine need for future intervention. CHD affects all racial, ethnic, and socioeconomic groups,² yet **underserved populations are disproportionately affected by disease-related morbidities**. For example, as compared to non-Hispanic White patients, Black and Hispanic patients are more likely to be delivered preterm, to be readmitted to the hospital after cardiac surgery, to exhibit neurodevelopmental and behavioral impairments, and ultimately, to die from CHD.^{3,6,7}

CHD is increasingly diagnosed prenatally across racial/ethnic groups.⁸ While prenatal diagnosis can be beneficial for the infant in that it facilitates medical care immediately following birth,^{9,10} **mothers describe their prenatal experiences as highly stressful and traumatic**.^{11,12} They report feeling terrified, isolated, hopeless, and emotionally unprepared.^{11,24} Mothers from underserved populations often experience added psychosocial risks (e.g., low health literacy, limited social support).¹⁸ Despite efforts in fetal cardiology to prepare parents for the medical aspects of CHD,⁹ efforts to directly address psychosocial aspects are severely lacking.

Maternal stress and trauma during pregnancy exert a powerful influence on birth outcomes and child neurodevelopment, particularly within vulnerable populations.¹³⁻¹⁵ Prenatal interventions to mitigate the negative effects of maternal stress have been shown to alter long-term developmental trajectories for children in underserved populations.²⁹⁻³² **Prenatal diagnosis of a birth defect, such as CHD, adds substantial stress and trauma for mothers during a critical time period, at a level of severity known to impact child outcomes.**¹⁶⁻¹⁸ A recent study of women carrying fetuses with CHD found that two-thirds experienced high stress, and prenatal stress/anxiety was associated with impairments in fetal cerebellar and hippocampal development.²¹ These associations were not observed for healthy fetuses, suggesting brain development for fetuses with CHD could be particularly vulnerable to in-utero effects of maternal stress. Other research suggests that maternal stress contributes to cognitive/language delays and emotional/behavioral dysregulation in children with CHD.^{19,20,22} Across CHD studies, maternal stress is a stronger predictor of child neurodevelopment than medical variables.^{33,34} Neurodevelopmental impairments disrupt academic achievement, social functioning, and family wellbeing, substantially altering long-term trajectories for these already vulnerable children and families.

A.2. RIGOR OF PRIOR RESEARCH. In light of evidence for the importance of maternal emotional wellbeing for the long-term developmental course of children with CHD, there have been numerous calls from clinical and patient/family communities to develop and test psychosocial interventions for this population.^{16-18,35} The few interventions tested to date were conducted postnatally with predominantly White, English-speaking mothers and were deemed to be at high risk of bias due to methodologic limitations.^{36,37} Our team has led community-engaged research aimed at understanding psychosocial needs of families impacted by CHD and preferences for intervention.^{11,24,38-41} Parents from diverse racial/ethnic and socioeconomic backgrounds, including Spanish-speaking parents, contributed their perspectives. **The need for psychosocial intervention soon after prenatal diagnosis to prevent negative effects for the family/child emerged as a consistent theme. Yet, to date there are no empirically supported prenatal psychosocial interventions for CHD or other birth defects.**

A.3. PRELIMINARY WORK. In partnership with diverse parents and multidisciplinary clinicians across eight pediatric health systems (*PEDSnet*), **our team recently designed *HEARTPrep*, an innovative, virtually-delivered prenatal psychosocial intervention for parents expecting a baby with CHD.** *HEARTPrep* will be delivered entirely through the Nemours App, a comprehensive and accessible mobile application for telehealth, education, and communication with clinicians. *HEARTPrep* was designed in accordance with the *ORBIT Model for Behavioral Treatment Development*,²³ a systematic framework for developing behavioral interventions through rigorous *Phase I* and *II* behavioral research. In our preliminary work (*ORBIT Phase Ia: Define*),²⁴ parents identified four outcomes that need to be addressed during the prenatal period to promote long-term maternal/family wellbeing: emotional distress (↓), social isolation (↓), parenting self-efficacy (↑), and



hope (↑). Parents and clinicians then identified intervention elements directly targeting these outcomes that can be flexibly delivered in a virtual format to overcome common barriers to intervention for this population (e.g., distance from hospital, competing demands). This work directly informed the design of *HEARTPrep*, which consists of three modules (*Adjusting, Connecting, Preparing*) and a suite of intervention elements (e.g., psychoeducation, psychotherapy exercises, peer support). Each module targets a distinct primary outcome (emotional distress, social isolation, parenting self-efficacy) and a common secondary outcome (hope) identified by parents as important for long-term maternal/family wellbeing. Based on our preliminary CHD research indicating that mothers and fathers express different needs and preferences for psychosocial intervention (e.g., fathers less likely to accept intervention focused on themselves, more likely to accept intervention they perceive will benefit their partner/family),^{11,40} expectant mothers will be offered *HEARTPrep*, and partners will be encouraged to participate together with mothers when appropriate. Our team also developed stakeholder-informed measures from PROMIS item banks⁴²⁻⁴⁵ to assess primary and secondary outcomes.

A.4. PROPOSED PROJECT. The proposed project will refine *HEARTPrep* and evaluate its impact for mothers expecting a baby with CHD. This study represents an important next step in Dr. Sood's research program, which has engaged the CHD community (parents, clinicians, advocacy groups) to improve outcomes for families by intervening at the time of CHD diagnosis.^{11,24, 38-41} Given the known challenges of delivering psychosocial interventions soon after diagnosis of a life-threatening condition,⁴⁶ **diverse parents of children with CHD have guided every step of the research** by helping to generate initial research questions, advising on recruitment/retention strategies, identifying meaningful outcomes, and determining intervention elements.

In alignment with the *ORBIT Model for Behavioral Treatment Development*,²³ we will (*Aim 1; ORBIT Phase Ib*) work with the Intervention Methods: Provision and Connection through Technology (IMPACT) Core to build *HEARTPrep* custom features into the Nemours App and refine it based on user feedback and (*Aim 2; ORBIT Phase IIa*) determine whether *HEARTPrep* produces clinically significant improvements.

B. INNOVATION

B.1. The *HEARTPrep* intervention is the first of its kind to directly target emotional wellbeing for mothers following prenatal diagnosis of a birth defect. Despite research connecting maternal stress and trauma during pregnancy to long-term developmental trajectories,^{13-15,21} there are no empirically supported prenatal psychosocial interventions for mothers of highly vulnerable children with birth defects. *HEARTPrep* has the potential to improve outcomes for children/families impacted by CHD. This intervention model can then be adapted for other birth defects (e.g., neural tube defects), given commonalities in maternal stress reactions and the disproportionate burden of disease-related morbidities in children from underserved populations.²⁶⁻²⁸

B.2. Use of a mobile app for intervention delivery is innovative. *HEARTPrep* will be delivered through the Nemours App, leveraging existing features (e.g., telehealth) as well as customization for this population (e.g., CHD educational tools). Intervention delivery via mobile app allows for an accessible intervention when and where parents need it most, transcending the constraints of traditional psychosocial interventions.

B.3. Weekly outcome assessment through an app is innovative. Administering repeated assessments will provide information on how outcomes change over time in response to *HEARTPrep* and inform optimized timing of user progression to the next module. No prior psychosocial intervention trials in CHD have utilized this assessment approach. An app is an ideal platform for weekly assessment given the ability to alert participants when an assessment is due and obtain outcomes from any location.

B.4. Outcomes and intervention elements were identified/designed in partnership with diverse parents, including Spanish-speaking parents, whose children received care across eight health systems (*PEDSnet*).²⁴ The critical role of patients/families in co-producing healthcare services has been increasingly recognized,⁴⁷ yet patients/families are rarely included as partners in the design of psychosocial interventions. In partnership with the Pediatric Research Optimizing Methods in Stakeholder Engagement (PROMISE) Core and the patient advocacy organization, *Conquering CHD*, diverse parents will be identified to serve as research partners for this project, increasing the likelihood that *HEARTPrep* will be feasible, usable, acceptable, and efficacious.

C. APPROACH

C.1. OVERVIEW. The proposed project will refine and evaluate *HEARTPrep*, a novel psychosocial intervention for mothers expecting a baby with CHD delivered through the Nemours App. Participants will be recruited from two hospitals within the Nemours Children's Health System in Delaware and Florida. Most research activities will occur in Delaware (e.g., virtual intervention delivery). Team members in Florida (in-kind contribution) will assist with in-person recruitment/enrollment and Aim 1 Think Aloud testing for Florida

participants.

C.2. RESEARCH TEAM. Dr. Sood, research project leader, is a pediatric psychologist in the Nemours Cardiac Center and Center for Healthcare Delivery Science and Associate Professor of Pediatrics at Thomas Jefferson University. She is a junior investigator with a strong track record of funding for her research on family-based psychosocial interventions for CHD through foundation, pilot, and mentored career development (K12) grants. Dr. Sood is highly active in the CHD community, serving as Co-Chair of the Cardiac Neurodevelopmental Outcome Collaborative (2018-2020) and medical advisor to multiple patient advocacy organizations. **Dr. Sood has assembled a mentorship team (Kazak, Forrest, Laurenceau, Deans) comprised of international experts** in medical traumatic stress, family-based psychosocial intervention, stakeholder-informed intervention design, patient-centered outcomes research, and intensive longitudinal methods.

C.3. INTERVENTION. HEARTPrep consists of three distinct modules: Adjusting, Connecting, and Preparing. Modular approaches to intervention are well established and have strong empirical support for a wide range of conditions.⁴⁹⁻⁵⁴ Defining features of modularity in the design of interventions include: 1) the intervention can be divided into meaningful functional units (i.e., modules) each with a specified purpose, 2) the operation of each module is expected to produce the intended result (i.e., primary outcome), and 3) modules connect with each other in a structured fashion (i.e., rules for transitioning between modules).⁴⁹ Modular approaches can be particularly useful for individuals with multiple interrelated problems (i.e., multiple outcomes). Each module can target a different problem by applying those intervention elements known to be effective for the problem, typically more efficient and practical than targeting each problem through separate interventions.⁴⁹

Each HEARTPrep module targets one distinct primary outcome (emotional distress, social isolation, parenting self-efficacy) and a common secondary outcome (hope) through a suite of evidence-based intervention elements (e.g., mindfulness, psychoeducation, cognitive restructuring) for addressing emotional problems in other populations, including pregnant women.⁵⁵⁻⁵⁹ Many of the elements are included within well-established, empirically-based intervention approaches (e.g., cognitive-behavioral therapy, interpersonal psychotherapy).⁶⁰⁻⁶² HEARTPrep elements will be delivered virtually in English and Spanish through a) telehealth with a psychosocial provider, b) recorded videos, c) educational tools, and d) links to resources. In our preliminary work, parents of children with CHD (including Spanish-speaking mothers) rated HEARTPrep elements as acceptable and likely to impact outcomes. Given the interrelated nature of the outcomes and our assumption that modules will interact to produce a whole with better functioning than the sum of its parts,⁴⁹ we expect all three modules to impact all outcomes, with greatest impact during the module targeting that outcome.

HEARTPrep Elements <i>Mode of Delivery</i>	Module 1: ADJUSTING	Module 2: CONNECTING	Module 3: PREPARING
Psychoeducation <i>Telehealth, educational tools</i>	Normalize distress/grief, provide education on emotional adjustment process	Normalize interpersonal challenges, provide education on common patterns	Normalize fears/insecurities, provide education on common behavioral responses
Psychotherapy exercises <i>Telehealth, educational tools, links to resources</i>	Relaxation exercises (deep breathing, progressive muscle relaxation)	Cognitive-behavioral exercises (cognitive restructuring, problem solving)	Mindfulness/acceptance exercises (five senses, leaves on a stream)
Engaging support network <i>Educational tools, telehealth</i>	Tips to share with family/friends on providing support after CHD diagnosis	Strategies to enhance communication and improve interpersonal functioning	Strategies for engaging support network after the birth and in hospital
Peer-to-peer support <i>Recorded videos, links to resources</i>	Personal stories/videos about emotional adjustment process, links to peer support options	Personal stories/videos about interpersonal challenges, links to peer support options	Personal stories/videos about preparing for a baby with CHD, links to peer support options
Exploring role of cultural beliefs and/or faith <i>Telehealth</i>	Role of cultural beliefs/faith for emotional adjustment	Role of cultural beliefs/faith for feeling connected/less alone	Role of cultural beliefs/faith for feeling prepared and hopeful
CHD educational tools <i>Educational tools, recorded videos, links to resources</i>	Glossary of common medical terms, links to trusted websites	Guided questions tool (to facilitate interactions with medical providers)	Expectant parent videos (preparing for birth/surgery, caring for baby in hospital)

Each HEARTPrep module is designed to take approximately 4 weeks to complete (12 wks total: ~24-36 weeks gestation). However, duration will be individualized (± 2 wks) based on review of outcomes and mothers' perceived needs. For example, the process of adjusting to CHD diagnosis will likely vary and some mothers may benefit from less (2 wks) or more (6 wks) time in the *Adjusting* module. For those who progress through all modules in <12 weeks, a booster session to review intervention elements will occur ~36 weeks gestation. Mothers who spend >4 weeks in either of the first two modules will transition to the last module no later than 34 weeks to ensure sufficient time on this content. **While expectant mothers are the primary HEARTPrep users,**

partners can also participate based on maternal preference and individual family needs. Partners can access custom *HEARTPrep* features within the App and participate in telehealth sessions together with mothers.

***HEARTPrep* will be delivered through the Nemours App installed on the participant's mobile device** (i.e., smartphone, tablet, laptop). Approximately 95% of adults in the United States of childbearing age across racial/ethnic and socioeconomic groups own a smartphone.⁶³ The Nemours App is a state-of-the-art mobile application and core component of Nemours' commitment to deliver healthcare how and when patients/families need and want it. It is available free of charge and currently in use by over 75,000 users for telehealth, education, communication with medical providers, and access to the medical record. Custom features have previously been built into the Nemours App for home monitoring of infants with CHD following cardiac surgery and are used successfully in Cardiology, including with mothers from underserved populations. This project will leverage existing features of the Nemours App (e.g., telehealth) while customizing the dashboard and content for *HEARTPrep* (e.g., educational tools, videos) in partnership with the IMPACT Core. In our preliminary work, parents who previously received a prenatal diagnosis of CHD rated the use of an app to deliver *HEARTPrep* as highly acceptable and preferred over in-person and paper formats. The App is integrated with Epic (a widely used electronic health record),⁶⁴ facilitating its transportability to other health systems in the future.

C.4. STUDY DESIGN.

Participants & Sampling: Participants for Aim 1 Think Aloud Testing will be mothers (ages 18+) who received a prenatal diagnosis of CHD within the last year, including expectant mothers who are currently pregnant and mothers who have been pregnant within the 12 months. Their partners will also be invited to participate. Participants for Aim 1 Beta Testing and Aim 2 will be expectant mothers (ages 18+) carrying a fetus identified as having CHD and receiving fetal cardiac care through a hospital within Nemours Children's Health System: Nemours Children's Hospital, Delaware (Wilmington, DE) or Nemours Children's Hospital, Florida (Orlando, FL). Recruitment will occur after expectant mothers decide they will continue the pregnancy, typically decided by 24 weeks gestation. Consistent with established guidelines for supporting partner involvement in prenatal care to promote positive maternal/family outcomes,⁶⁵ partners of participating mothers will also be invited to participate when mothers feel including their partner would be beneficial (e.g., for promoting maternal engagement in *HEARTPrep*, for promoting positive maternal/family outcomes). However, given limited prior research on partner outcomes following their involvement in prenatal interventions,⁶⁶ particularly for underserved populations,^{67,68} maternal outcomes will be primary and partner outcomes will be exploratory. Participants must speak English or Spanish and their baby must be expected to require cardiac surgery within the first year of life. Participants will be paid for their time (e.g., Think Aloud Testing: \$50; Post-intervention interview: \$50; *HEARTPrep* telehealth sessions: \$10).

Aim 1: Refine *HEARTPrep* and evaluate initial feasibility, usability, and acceptability.

Aim 1 consists of two parts: Think Aloud Testing and Beta Testing. Think Aloud Testing will be considered complete when no novel suggestions for improvement are identified (i.e., saturation), expected within 15-20 participants. Eligible expectant mothers/partners will be consecutively recruited for Beta Testing as the intervention is being iteratively refined. It is possible that the same expectant mother/partner may be eligible for both Think Aloud Testing and Beta Testing based on meeting the inclusion criteria for both. In these cases, mothers/partners will have the option of participating in one or both parts based on their preferences.

Recruitment (Think Aloud Testing): 15-20 mothers (and partners when applicable), including expectant mothers between 24-36 weeks gestation, will be recruited to participate in Think Aloud testing. They will be informed of the study by phone, and the consent process and Think Aloud testing will occur in person adjacent to a clinic visit. Mothers/partners can choose to participate together or separately.

Data Collection (Think Aloud Testing): Think Aloud testing is an established process in usability research to obtain in vivo feedback from users about a new tool/approach²⁵ and has been used successfully by members of the IMPACT Core for the development of e-Health interventions for English and Spanish-speaking families.⁷¹ After a brief introduction to *HEARTPrep*, participants will be instructed on how to install the Nemours App on their mobile device and oriented to the App and custom *HEARTPrep* features. A trained team member will then facilitate Think Aloud testing in English or Spanish (~30-45 mins). Participants will be instructed to say everything they are thinking and doing as they navigate through *HEARTPrep* to provide insight about their thought processes and decisions.⁶¹ Participant responses will be recorded/transcribed. A modified cognitive interview analysis protocol will be used to summarize participant feedback and make decisions about changes based on participants' understanding and interpretation of *HEARTPrep*'s design and content.^{71,72} Think Aloud testing will be iterative, with real-time changes made between participants in response to feedback. Testing will conclude when no novel suggestions for improvement are identified (i.e., saturation), expected within 15-20 participants.⁷¹

Additional participants will be recruited as needed to reach saturation.

Recruitment (Beta Testing): 40 expectant mothers (and partners when applicable) will beta test the intervention as it is being iteratively refined. Potential participants will be recruited and consented during a prenatal clinic visit or by phone.

Intervention Delivery & Data Collection (Beta Testing): Participants will be instructed on how to install the Nemours App and oriented to the App and custom *HEARTPrep* features. *HEARTPrep* will be initiated at approximately 24 (± 2) weeks gestation. To assess feasibility, usability, and acceptability, participants will complete a semi-structured, qualitative interview by phone/video at the end of the intervention. They will also complete the *HEARTPrep* Evaluation Survey after session 3 and again at the end of the intervention if the participant completes more than three sessions. The *HEARTPrep* Evaluation Survey was adapted from an existing survey used extensively to evaluate acceptability of a virtually-delivered intervention for parents of children with cancer.⁷¹ Mothers and partners will complete interviews/surveys independently. At the end of *HEARTPrep*, participants will also complete a brief (~30 minutes) semi-structured interview by phone about perceived acceptability and feasibility of *HEARTPrep* and the potential need for individualized intervention elements. Interviews will be recorded and transcribed with any identifiers removed. Mothers/partners will complete all assessments/interviews independently. App usage data (e.g., # telehealth sessions completed, educational tools reviewed) will be obtained through the app. Refinements needed to improve feasibility, usability, and acceptability based on interview/survey/usage data will be made iteratively until data indicate that *HEARTPrep* is feasible, usable, and acceptable for diverse expectant mothers (i.e., no consistent user issues identified from interviews, $\geq 80\%$ of participants responding *mostly true* or *very true* to each Evaluation Survey item, $\geq 80\%$ of telehealth sessions completed/educational tools reviewed). If a sample size >10 is needed to achieve this, additional participants will be enrolled.

Aim 2: Determine whether *HEARTPrep* modules produce clinically significant improvements on outcomes in mothers expecting a baby with CHD (Proof-of-Concept).

Recruitment: 40 expectant mothers (and partners when applicable) will be recruited and consented during a prenatal clinic visit or by phone. Estimating 65% enrollment, recruitment goals will be met in ~12 months. Expectant mothers who enroll will complete the procedures described below.

Intervention Delivery & Data Collection: Expectant mothers who consent for participation in *HEARTPrep* will be instructed on how to install the Nemours App, followed by orientation to the App and custom *HEARTPrep* features. *HEARTPrep* will be initiated at approximately 24 (± 2) weeks gestation. Telehealth sessions will be conducted by one of three *HEARTPrep* interventionists in English/Spanish.

Measures: Weekly assessment consists of questionnaires assessing the primary outcome for each module (emotional distress, social isolation, parenting self-efficacy) and common secondary outcome (hope). Weekly questionnaires will be administered through the Nemours app.

Parent Advisors. Six to eight parent advisors will provide their perspectives on priorities for future *HEARTPrep* research, data collection methods, selection of measures, and other topics relevant to this line of research. Parents serving in this role may have previously participated in *HEARTPrep* research, but are not current participants. Importantly, they will have no access to study data or participant information or identifiers. This activity does not meet the definition of research participation nor do they meet the criteria for research team members. Parent advisors will provide feedback through phone calls, Microsoft Team meetings, or emails. They will be paid \$50 per hour dedicated to the project.

C.5. DATA ANALYTIC PLAN. Beta Testing (Aim 1). Themes from qualitative interviews will be identified using an inductive thematic approach.⁷⁹ Quantitative data on feasibility, usability, and acceptability will be analyzed via descriptive statistics. **Proof-of-Concept Trial (Aim 2).** Visual analysis of time-series data (weekly outcomes) from expectant mothers will be used to assess reliability and magnitude of intervention effects.^{80,81} We expect the primary outcome for each *HEARTPrep* module to respond differentially to the introduction of that module (i.e., piecewise growth curve model with pieces of different slopes linked together by turning points).⁸²

C.6. POTENTIAL PROBLEMS/ALTERNATIVES. Recruitment soon after CHD diagnosis and retention throughout pregnancy could be challenging. While parents who previously received a prenatal CHD diagnosis helped to design *HEARTPrep*, distress may prevent expectant mothers from enrolling or engaging. Such challenges will be identified and discussed with the study team, including parents, and we will optimize processes to promote recruitment/retention (e.g., timing of recruitment, flexibility in telehealth scheduling). Recruitment of diverse parents can also be challenging. Our group has had success with using purposive sampling to enroll diverse parents in CHD research (including Spanish-speaking parents),^{11,24} and we will rely on this strategy to

ensure diverse samples. We will access resources through the IMPACT Core for expertise in intervention development for Spanish-speaking populations. Research activities could be impacted by COVID-19. Fetal cardiac care at Nemours has continued in-person throughout the pandemic and the number of eligible mothers should not be affected. Given the virtual nature of *HEARTPrep*, study aims can be achieved without in-person research activities. Mothers are primary *HEARTPrep* participants, with partners also encouraged to participate. Based on our preliminary data indicating that many mothers prefer not to involve extended family in prenatal psychosocial intervention, other family members will not be included. However, this could be revisited if results from the proposed study indicate the need to include extended family. Technological advances are likely to result in changes to the Nemours App over time. We will work with the IMPACT Core to ensure that *HEARTPrep* can be delivered while leveraging advances in technology. Importantly, the Nemours App is integrated with Epic (a widely used electronic health record),⁶⁴ facilitating its transportability to other health systems in the future.

C.7. SCIENTIFIC RIGOR. This study was designed in accordance with best practice recommendations for developing psychosocial interventions for chronic disease populations. We have aligned study aims with ORBIT Model phases of intervention development,²³ building on our extensive preliminary research.^{11,24,38-41} We will use Think Aloud Testing, an established tool in usability research,²⁵ and qualitative interviews to inform refinements to *HEARTPrep*. All qualitative data will be coded/analyzed using established methods.⁸⁴ Planned sample sizes for Aims 1-2 are based on research suggesting that prototype refinement can be accomplished with 15-20 participants^{71,85,86} and a sample size of 20 is typically sufficient to demonstrate proof-of-concept.⁸⁰ We developed weekly assessment measures from PROMIS item banks with demonstrated validity/reliability.⁴²⁻⁴⁵ We will employ rigorous analytic approaches and follow transparent reporting guidelines to enhance reproducibility.⁸⁹⁻⁹¹

C.8. FUTURE DIRECTIONS. This study will position Dr. Sood well to secure external funding for multi-site evaluation of *HEARTPrep*. With a refined stakeholder-informed intervention and preliminary data, Dr. Sood will be a highly competitive applicant for funding from NIH and PCORI. This model of intervention could then be adapted and tested with other birth defects (3% of all births), filling critical gaps in support for vulnerable families and influencing outcomes of future generations.