Study Title: Improving COVID-19 Vaccine Uptake Using mHealth Tools: A Qualitative Study

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Study location: Sites within the IDeA States Pediatric Clinical Trials Network (ISPCTN)

Summary of Key Changes

Version 03 to Version 04

Section(s)	Summary of Revisions (V-03 to V-04)	Rationale
Title page	Added James Roberts as an additional Lead Study Investigator	Correction
Schedule of Activities	Added "x" for week 8 for focus groups and key informant interviews	Correction
Inclusion Criteria – Race/Ethnicity	Clarified race/ethnicity inclusion criteria	Study clarification
Participant Recruitment – Retrospective	Changed 12 months to 24 months in the following sentence. The practice will develop the list from 24 months of patient-visit data (e.g., billing records).	Correction
Pre-Interview Survey	Removed zip code from demographic data collected	The study team determined this data does not need to be collected.
Interview Procedures: General Procedures	Added: "and will schedule around participants availability"	Clarification
Focus groups and Figure 1	Changed the number of participants in focus groups and the number of participants recruited for focus groups Specifically, decreased the maximum recruitment number from 12 to 8 per focus group and decreased focus group participant size FROM "8 to 12" TO "5 to 6".	Study team determined that focus groups should be smaller
Rescheduling	Added subsection to describe that focus groups and interviews can be rescheduled and that participants will be contacted to reschedule, if necessary.	Procedure addition

Version 04 to Version 05

Section(s)	Summary of Revisions (V-04 to V-05)	Rationale
Title page	Changed contact Information for Dr Darden	Correction
Payment to Research Participants	Created a new section specific to participants payment, moved sentence participants payment and added additional language about modality of payment	Created new section and Added specific language
Data Coding and Analysis	Added language to indicate that research team will use other software rather than only "textinspector" for data analysis	Additional language

Version 05 to Version 06

Section(s)	Summary of Revisions (V-05 to V-06)	Rationale
Participant Recruitment	Change made to state that individual that do not wish to be contacted about the study, should contact the research staff (not the practice).	Correction
Participants Recruitment_ Retrospective paragraph:	Changed "2 years" to "24 month" Added "designees" and "or research staff"	Change and Addition
Enrollment and Informed Consent Process	Added "designees" as other research staff involved in specific study-related procedures.	Addition
Participant Screening and Enrollment_	Added video call as a method to conduct the pre-interview survey. Typo correction Clarifying that before completing the pre-interview survey research staff will obtain consent as previously described.	Addition, Correction. Deletion and Clarification
Interview Procedures	Changes to specify that a contracted transcription service system will be used to generate transcripts of recorded discussions. Added possible "similar sites" suggested to participants to learn more about vaccination. Added "designees" as other research staff involved in specific study-related procedures.	Change and Addition
Quality Assurance	Correction "moderators" to "facilitators" Deleted sentence about certification of Spanish translators.	Deletion and Clarification
Site Responsibilities	Added "designees" as other research staff involved in specific study-related procedures.	Addition

Section(s)	Summary of Revisions (V-05 to V-06)	Rationale
Key Informant and Focus Group Interviews	Added “study team member” as other research staff involved in specific study-related procedures. Deleted “automated” referring to transcription system	Addition and Deletion
Pre-Interview Survey	Changed to specify that site research teams will have access to the contact information to schedule the focus group or individual interview	Change

Section(s)	Summary of Revisions (V-06 to V-07)	Rationale
Schedule of Activities	Revision of timeline table to extend timeline for study procedures	Addition
Key Informant Interview	Deletion of sentence referring to the maximum number of participants that will be consented in order to conduct 8 individual interviews. Addition of language referring to research team maintaining a “wait list” of participants for rescheduling.	Deletion and Addition
DCOC Responsibilities	Additional responsibility to ensure that transcript of discussions is de-identified.	Addition

Background and Rationale

Objective

Our research objective is to conduct a qualitative assessment of the constructs that influence parental Coronavirus Disease 2019 (COVID-19) vaccination decision-making for children in rural and underserved communities. Data from this formative study will guide content development for an eventual mHealth tool that will be tested for its impact on pediatric COVID-19 vaccine uptake.

Public Health Impact

COVID-19 Vaccines for Children

From December 11 through May 10 2021, the US Food and Drug Administration (FDA) expanded the emergency use authorization (EUA) of the COVID-19 vaccine for individuals and adolescents as young as 12 years of age. By the end of 2021, children as young as 2 years of age could be eligible for the COVID-19 vaccine. SARS-CoV-2, the virus that causes COVID-19 disease, infected more than 3 million children and killed more than 300 children. High COVID-19 vaccination coverage among children is critical to lessen the public health burden on children's physical, mental, and social health.[1,2]

Epidemiology of COVID-19 Vaccine Hesitancy

The WHO defines vaccine hesitancy as the delay in acceptance or refusal of vaccination, despite availability of vaccination services.[3] This definition includes decisions, behaviors, and cultural factors related to vaccines,[4] but excludes factors such as failure of communication, lack of access, and the absence of an offer of vaccine. Thomson, et al proposes another operational definition that includes these factors and frames these factors around 5 As; access, affordability, awareness, acceptance, and activation (i.e., motivation to act).[5]

The currently approved COVID-19 vaccines in the United States demonstrate excellent effectiveness (66-95%) against infection and symptomatic disease, and more importantly almost 100% protection from severe disease and death.[6,7] However, nearly 4 in 10 Americans state they probably or definitely will not get vaccinated and many states in the Institutional Development Award (IDeA) Program have higher rates of COVID-19 vaccine refusal, compared with non-IDeA states.[8] A nationwide survey of adults shows that as of May 2021, 37.3% of US adults were already fully vaccinated against SARS-CoV-2. Nonetheless, from June 2020 to February 2021, the percentage of adults who were "extremely unlikely to be vaccinated"

rose from 12% to 17%. When asked, "If you were able to choose when to get a COVID-19 vaccine, would you get it?" there was substantial variation by state in the prevalence of adults who responded that they "would not get the COVID-19 vaccine," with Oklahoma and North Dakota having the highest percentage of refusers at 33%. Other states within the IDeA States Pediatric Clinical Trials Network (ISPCTN) also had high prevalence of refusers including West Virginia (30%), New Mexico (30%), Mississippi (31%), Louisiana (30%), and Arkansas (31%).[9] When asked in this same survey about their level of acceptance of COVID-19 vaccine for their children, parents of teens were less resistant than parents of younger children, and mothers were more resistant than fathers. Parents in households making < $25,000, without college degrees, and who self-identified as Republicans were also less likely to vaccinate their children.[10]

Several other surveys have found that individuals from African American and Hispanic communities express higher COVID-19 vaccine hesitancy, despite experiencing significantly worse disease burden and mortality.[11-14] African American adults have shown mores suspicion and lower confidence in vaccines, and are 41% more likely than Whites to refuse a COVID-19 vaccine.[15] Similarly, Non-Hispanic Blacks are 46.7% more likely to express intent not to vaccinate than non-Hispanic Whites (30%).[16] Rural (non-metro) respondents were 40% more likely to express intent not to vaccinate than urban (metro) respondents (30%).[16] Rural residents are also less likely to report that they are planning or considering COVID-19 vaccination;[17] this is particularly true for Whites and Republicans. Rural African American, however, report difficulty in accessing the vaccine.[17] Interestingly, Hispanic respondents were not different from Whites in intent not to vaccinate (32% versus 30%).[16]

The NIH has identified these vulnerable populations, as well as individuals from rural, medically underserved, and migrant communities, as high priorities for vaccination and vaccine communication efforts.[18] Key goals of vaccine communication highlighted by the NIH include: (1) providing assurance of vaccine safety; (2) highlighting collective and individual benefits to vaccination; (3) explaining the vaccine development and approval process; (4) addressing vaccine hesitancy; and (5) monitoring and countering misinformation. To be effective, these communication objectives require tailoring to specific target audiences and must therefore (1) leverage close community partnerships to identify relevant information needs and cultural context; and (2) employ scalable and impactful communication strategies that encourage vaccination across diverse segments of the population.

This study proposes to address these knowledge gaps:

- Parental attitudes toward COVID-19 vaccine by race/ethnicity and rurality.
- Parental attitudes regarding acceptance of COVID-19 vaccines for their children as compared to themselves.

- Potential ways to address COVID-19 vaccine hesitancy in parents.

Information to be collected can inform the content of an eventual mHealth application (app) designed to support parental acceptance of COVID-19 vaccine for their children.

Harnessing mHealth to Support Parental COVID-19 Vaccine Acceptance

mHealth tools, such as mobile apps and decision support tools, demonstrate the potential to positively impact vaccination rates.[19] Tools that increase healthcare providers' knowledge and self-efficacy with vaccines can increase rates of vaccine initiation and completion, but current tools face limitations in scalability and assessing actual utilization of the intervention.[20] Members of our team have developed mHealth tools to address vaccine hesitancy of healthcare providers, which have demonstrated improvements in randomized trials.[21] Additionally, members of our team have extensive experience developing and deploying customizable mobile electronic clinical decision support tools for use by healthcare providers. These tools have been used by >20,000 users and incorporate user analytics that enable assessment of engagement with the tool.[22-24] We have also created customizable mHealth tools for COVID-19 infection response for families that, in partnership with community stakeholders and school districts, have been translated into multiple languages, including English, Napoli, and Spanish. Preliminary data since its release in August 2020 show that these tools demonstrate broad uptake and use across diverse racial and ethnic groups.[15-17] Given that healthcare providers and families from underserved communities broadly use smart phone and mobile devices,[25,26] mHealth interventions hold the promise of broad uptake to these populations in the midst of a pandemic with limited face-to-face interventions. Additionally, through our ability to customize our tool in partnership with high-trust community organizations and institutions, our tool holds the promise of effectively involving diverse audiences in considering thoughtfully tailored COVID-19 vaccine messaging.

Frameworks for Studying Vaccine Attitudes and Behaviors

Interventions in behavioral change have been studied using a variety of frameworks. For example, the Theoretical Domains Framework was used in a recent Canadian study analyzing 605 relevant tweets to identify reasons behind vaccine hesitancy.[27,28] That study, similar to most Twitter data, used content analysis, which allows content grouping by themes to understand vaccine knowledge, attitudes, and beliefs.[29] Nearly half of the tweets expressed concerns about vaccine safety, including fear of vaccine side effects and potential lack of rigor in vaccine development; just over 25% of the tweets suggested a lack of science-based understanding of vaccines by the author.

To guide the proposed qualitative assessment, we will use the Consolidated Framework for Implementation Research (CFIR)[30] as a means for mapping territory that emerges from participant responses. As analysts of grounded theory suggest,[31] our pursuit of theory will be grounded in our engagement with the data generated from interviews. Our research question for this study asks: For each of the five domains of CFIR (listed below), what themes that parents raise provide reasons that would facilitate or inhibit full program implementation over time for parents considering COVID-19 vaccination? The CFIR five domains are: intervention characteristics, outer setting, inner setting, characteristics of the individuals involved, and the process planning for potential implementation of the app in future.[32] For this study, the intervention to be evaluated is COVID-19 vaccination in children <18 years of age. Constructs within CFIR domains to be explored if relevant to vaccine decision making include:

1. Intervention Characteristics: Evidence strength and quality, relative advantage, adaptability, perceived complexity
2. Outer Setting: Patient needs and resources, external policies and incentives and peer pressure
3. Inner Setting: Structural characteristics, social network composition and characteristics, culture, implementation climate/access
4. Characteristics of Individuals: Knowledge and beliefs about the vaccine, self-efficacy, individual stage of change, individual identification with organization, and other personal attributes
5. Process: Evidence of planning, engaging, executing, reflecting and evaluating vaccine decision

Method: Constructivist Grounded Theory

Since parental perceptions about COVID-19 vaccine communication are relatively unknown, this study will use constructivist grounded theory in the tradition of Charmaz[33] to explore knowledge, attitudes and beliefs that contribute to vaccination decisions. This qualitative approach suits exploratory studies where the concentration centers on how participants make sense of their experience and where participants may have a variety of perspectives in constructing a social event, such as deciding about COVID-19 vaccination for their children in the context of their social environment. The purpose of this qualitative analysis that will use focus groups for data collection is to represent a set of opinions and perceptions from each group, rather than aim at some representational sample more suitable for generalizing.[34] Similar to the qualitative interview approach,[35] the focus group approach[36] follows principles and methods established for effective conversational interaction associated with this type of data collection: setting ground rules for expectations of group conduct; using a set of semi-structured, open-ended questions developed to prompt description, reflection, and elaboration;

gathering feedback on questions from the research team for revision and rigor; and using question sequence designed to build rapport and support the flow of information. Importantly, the specific goal of this study is to inform the mHealth intervention trial in ECHO ISPCTN, which will focus primarily on rural Caucasian and rural or urban Latinx and African American communities with access to an electronically delivered intervention. While the broad themes identified may be generalizable to other settings, the study population and approach are specifically focused on the needs of the full-scale trial.

Long-Term Goal

Our long-term research objective is to develop a usable and scalable vaccine electronic communication tool that increases pediatric COVID-19 vaccination prevalence in diverse US communities to reduce COVID-19-related morbidity and mortality overall, and disparities in COVID-19 outcomes by sociodemographic background. Our rationale for this study is that its successful completion will identify interventional, environmental, organizational, individual, and process-specific factors that maximize and sustain engagement in vaccination initiation and completion. This assessment will inform future scalable rollouts of vaccine communication programs.

Study Design and Procedures

Schedule of Activities

Activity	2-week run-up	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	Week 13	Week 14	Week 15
Send opt-out letters; Receive & organize patient lists	x															
Recruitment		x	x	x	x	X	X									
Focus groups*		x	x	x	x	x	x	x	x	X	X	X	X	X		
Key informant interviews*		x	x	x	x	x	x	x	x	X	X	X	X	X		
Translation, transcription, coding, & analysis*		X														
Interim report																

* Given the nature of the study, the schedule of activities represents good-faith estimate for timing of activities. Sites will not simultaneously begin the two-week run-up. Focus groups, key informant interviews, and translation, transcription, coding, and analysis could start as early as week 1. The study team will hold or reschedule focus groups and key informant interviews based on participant enrollment. Translation, transcription, coding, and analysis will begin as soon as transcripts and data are available.

Overall Study Design

The study team proposes a qualitative study. Specifically, we will conduct a series of key informant and focus group interviews. Individual interviews (key informant) will be conducted with a limited number of parents who have already established strong opinions as to whether to vaccinate their child against COVID-19 (vaccine acceptors and refusers). Focus groups will be conducted with a greater number of parents who are still deciding (vaccine hesitant). More vaccine hesitant than acceptors or refusers will be interviewed in focus groups because the vaccine hesitant are the primary target of the eventual mHealth tool that this preliminary study intends to inform; nonetheless, eventual education and support of the vaccine hesitant requires some understanding of decision drivers among acceptors and refusers.

This qualitative study will be used to generate audience-specific messaging on the mHealth tool that will be tailored to address typical COVID-19 vaccination knowledge and motivational gaps as well as logistical barriers among rural and underserved African American, White, and Hispanic parents, respectively. We are focusing primarily on these populations in this study given their reported heightened vaccine hesitancy;[10-14] however, we will not exclude participants identifying with other races and/or ethnicities. We anticipate that provider recommendation will be one of the key aspects of increasing vaccine acceptance, and the study team will recruit participants from clinics. Sites will recruit parents/caregivers from each participating practice to participate in semi-structured interviews and focus groups.

Study Population

Sites

The study team will choose 4 clinical sites or networks within the ISPCTN states that have an existing research relationship with an ISPCTN awardee site and can demonstrate that they care for enough pediatric patients that meet the inclusion criteria. Sites must be able to recruit up to 20 Spanish-speaking participants and be able to recruit participants from each of the demographic/ethnicity groups described below. Sites must also be able to guarantee 50% site research coordinator effort for 1 month.

To ensure sufficient population size for recruitment, the study team will select among clinics that provide general healthcare to a minimum of 100 pediatric patients per year. Given that primary pediatric care in rural settings often occurs in family medicine clinics, including these clinics as potential sites will increase generalizability of our findings.

Participants

The populations targeted for the current study and for the eventual mHealth interventional trial will be adult, custodial parents/caregivers of children ages 2 to 17 years. The targeted populations will include members of sociodemographic backgrounds disproportionately affected by COVID-19-related morbidity and mortality, as described below.

Inclusion Criteria

- **Child/children are 2-17 years old.** At the time of consent, parents/caregivers must be the legal guardian for at least one child aged 2 to 17 years. At the time of screening and consent the parents/caregivers (participants) must have reached age of majority.
- **Internet connectivity.** The parent/caregiver must have access to a strong Internet connection and a device that can access an online conferencing platform, since interviews will be conducted virtually.[37]
- **Race/Ethnicity.** Parents who are: (1) non-Hispanic White rural; (2) Black/African American rural or urban; (3) Spanish speaking rural or urban, and; (4) participants who are rural and who are NOT non-Hispanic White or non-Hispanic Black.

Exclusion Criteria

- **Parent/caregiver has a developmental delay or cognitive impairment that could affect protocol compliance.** We will exclude parents/caregivers with a known developmental delay, as this could negatively affect participation.
- **Non-custodial parent/caregiver.** We will exclude parents/caregivers who are unable to give consent to vaccinate their child.
- **Non-English or Spanish speaking.** We will exclude parents/caregivers who do not speak English or Spanish, since the mHealth tool that the qualitative data will inform will only be available in these two languages.

Participant Recruitment

For efficiency, identification of potential participants will rely on several methods to capitalize on existing electronic medical record databases and clinical workflows at study recruitment sites. Proposed identification methods include retrospective lists of recently seen patients and traditional advertisements for self-referral.

Based on ISPCTN clinics' recent experience with patient recruitment, we expect that the retrospective list method will have the highest yield. To allow research staff to contact potential participants, we will send an opt-out letter to potential participants, which will come from the lead clinicians in the designated practices. This letter will describe the study and inform families that research staff from the participating sites will contact them. If families do not wish to be contacted, they will be asked to contact the research staff to opt out of the study.

- **Retrospective.** Site research coordinators (or other designated personnel) will identify potential participants by reviewing a list of pediatric patients provided by participating clinics who were seen consecutively by clinicians in the last 24 months and who meet the enrollment criteria. By accessing the medical records of pediatric patients, the site research coordinators/designees will collect the contact information of parents/caregivers. The practice or research site will develop the list from 24 months of patient-visit data (e.g., billing records). The site research coordinator/designee will organize this list from more to less recent clinic visit dates and remove duplicate patients. The generated list will include patient zip code and contact information (e.g., mail, e-mail, and phone number).
- **Traditional.** Sites may engage in traditional clinical trial recruitment methods focused on participant self-identification. Participants recruited through the traditional method do not have to be affiliated with the participating clinic. The Data Coordinating and Operations Center (DCOC) will provide a menu of options from which sites can choose, such as flyers, email, or advertisements on social media. The DCOC will obtain IRB approval for all recruitment materials. Recruitment materials will provide a link to contact site research coordinator/designee for more information or to complete a pre-interview survey, which begins with a short description of the research study and eligibility screening items.

Enrollment and Informed Consent Process

Site research coordinators/designees will contact potential participants and will perform the consent process by following the Information Sheet. The consent process may be conducted by call (video or telephone) or by e-mail. The Information Sheet will state the purposes, procedures, and potential risks of the study and describe participants' rights as research participants. Participants will have the opportunity to ask questions during the consent process, and if preferred, the site research coordinator/designee can send the Information Sheet to the participant and contact the participant after he or she has time to review the Information Sheet.

This is a minimal risk study and a waiver of documentation of consent is requested for the entire study. The research involves no procedures for which written consent is normally required outside of the research context.

The Facebook advertisements, poster, and flyer will contain a quick response code (QR code) that leads potential participants to the "pre-interview survey." The survey starts with a short description of the research study and states that if the participant is eligible for the study, the site research team will contact him/her with more information. At completion of the pre-interview survey, the site research team will receive contact information for eligible participants, and the team will contact eligible participants by phone/email to perform the consent process and schedule the focus group or interview session. The site research team will use the Information Sheet as phone script to perform the consent process.

The site research team will document the consent process as follows:

- For the pre-interview survey, the return of the survey will be considered as documentation of consent to participate.
- For the focus groups and individual interviews, participation will be considered as documentation of consent to participate.

The site research team will inform participants that participation is voluntary, that they may withdraw from the trial at any time without prejudice, and that nonparticipation will not adversely affect their medical care.

During the consent process, the research team will ask the participants if they would like to be contacted for future research.

Participant Screening and Enrollment

Screening

Site research coordinators/designees will screen participants via an online pre-interview survey that site research coordinators/designees will disseminate to potential participants via a REDCap link or similar HIPAA-compliant electronic data capture (EDC) system. Sites can also distribute the survey in a variety of ways: email, electronic medical record (EMR) direct messaging, social media, etc. Moreover, the site research coordinators/designees may perform the pre-interview survey with the potential participants by phone call and may directly enter the data in the designed EDC system. This pre-interview survey is minimal risk, does not involve procedures for which written consent is normally required outside of the research context, and is required to conduct the study. Therefore, the study team will request a waiver of the Health Insurance Portability and Accountability Act (HIPAA) authorization and documentation of

informed consent from the institutional review board (IRB) of record to identify potential participants from medical records and to conduct the pre-interview survey. Return of the survey will be considered documentation of consent to participate in the screening portion of the study.

The majority of the pre-surveys will be done by the research staff by phone or video call. The research staff will describe the research study to the potential participant using a short summary or IRB-approved scripts.

Pre-Interview Survey

The pre-interview survey will begin with a preamble stating that the study team is inviting the parent to participate in a short survey designed to identify participants for a focus group study or individual interview. The pre-interview survey will request consent (as previously described) to complete the questionnaire. This preamble will also state that the potential participant's care in the practice/clinic will not be affected by their decision to participate in the survey. The preamble will be provided in both English and Spanish so that participants may select their preferred language. The survey language will match the language the participant selects in answering the consent. The survey itself will consist of a short screening survey to assess parental interest in the COVID-19 vaccine and will continue on to items that ask demographic questions, including preferred contact information and self-identified race and ethnicity.

To avoid confusion for families who might have already gotten their child vaccinated to COVID-19, we will begin with the question: "Has your child already received a COVID-19 vaccine?" Yes/No. For those who reply No, we will use an item taken from the Rapid Acceleration of Diagnostics – Underserved Populations (RADx-UP) survey.[38]

How likely are you to vaccinate your child within the next 3 months?

1. Very likely
2. Fairly likely
3. Not too likely
4. Not at all likely
5. Definitely not

The study team will classify respondents choosing option 1 or 2 as "vaccine acceptors", those choosing options 3 or 4 as "hesitant", and option 5 as "vaccine refusers." Finally, parents will be asked for their

contact information, to confirm that they have internet connectivity that would allow participation in the focus groups or individual interview, and for their availability to participate in a future interview.

Interview Procedures

General Procedures

Key informant interviewers and focus group leaders will conduct all interviews and focus groups virtually on a videoconferencing platform (Zoom or similar videoconference system), primarily during evenings and weekends, and will schedule around participants availability. When necessary, the interviewers and focus group leaders will use a contracted transcription service system to generate initial transcripts of all focus groups and interviews. All focus groups and interviews will also be video (optional) and audio recorded for manual cleaning and verification of electronic transcripts. Participants will be allowed to not turn on their cameras during focus groups and interviews.

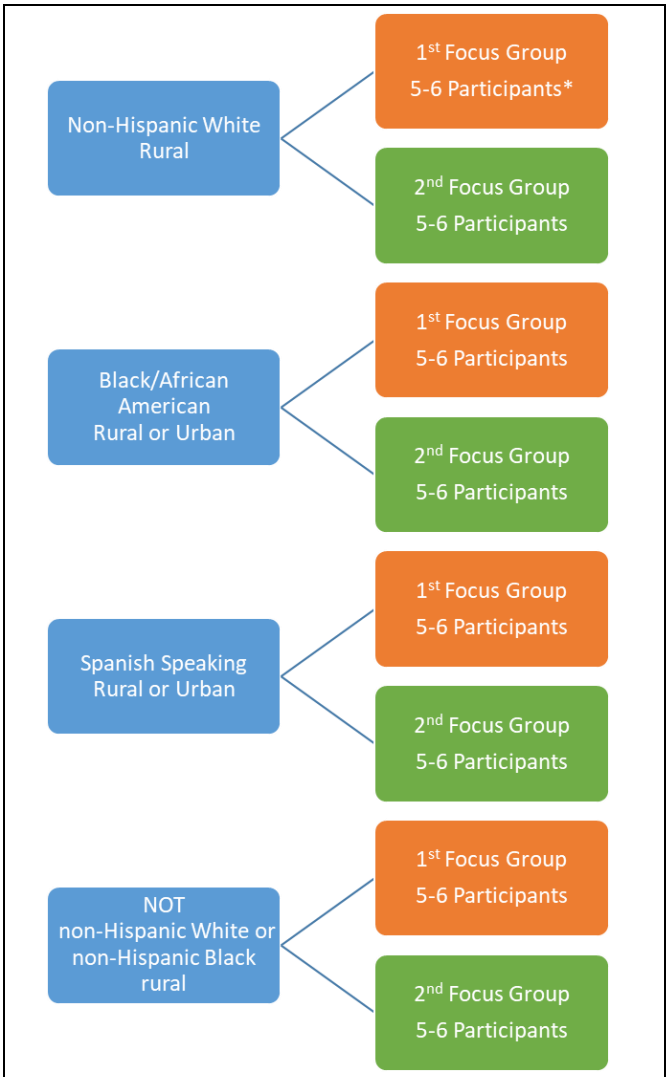

Figure 1. Focus groups per race/ethnicity group.*Will recruit up to 8 participants per focus group to account for cancelations and no-shows.

Participants will only participate in 1 focus group or key informant interview. After each key-informant and focus group interview, the study team will share links to websites from the Centers for Disease Control and Prevention (CDC) and American Academy of Pediatrics (AAP), or similar sites, with parental guidance on COVID-19 vaccines for children and teens (www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/adolescents.html and www.healthychildren.org/English/health-issues/conditions/COVID-19/Pages/The-Science-Behind-the-COVID- 19-Vaccine-Parent-FAQs.aspx)

Focus Groups. The study team will conduct focus groups with participants who identify on the pre-interview survey as "vaccine hesitant." Focus group leaders will conduct two focus groups per race/ethnicity strata (Fig. 1). Focus groups will consist of up to 5 to 6 participants from across participating sites. Site research coordinators/designees will recruit 7-8 participants per focus group to account for no-show participants. The study team will hold additional focus groups if thematic saturation is not reached in emerging analysis. The participant size range for each focus group is consistent with optimal representation in focus group studies, where persons appointed may not show up and a sample should not be too large for active involvement in a discussion. With participants categorized as "hesitant" on the pre-interview survey, the study team will conduct focus groups. Focus groups will be stratified by race/ethnicity as well as rurality. There will be capacity to conduct a Spanish-language focus group if there are sufficient numbers of potential participants to warrant it. See the focus group guide for possible questions and probes. Actual questions for each focus group may vary depending on the flow of conversation and questions may evolve over the course of the study according to the findings of ongoing constructivist ground theory.

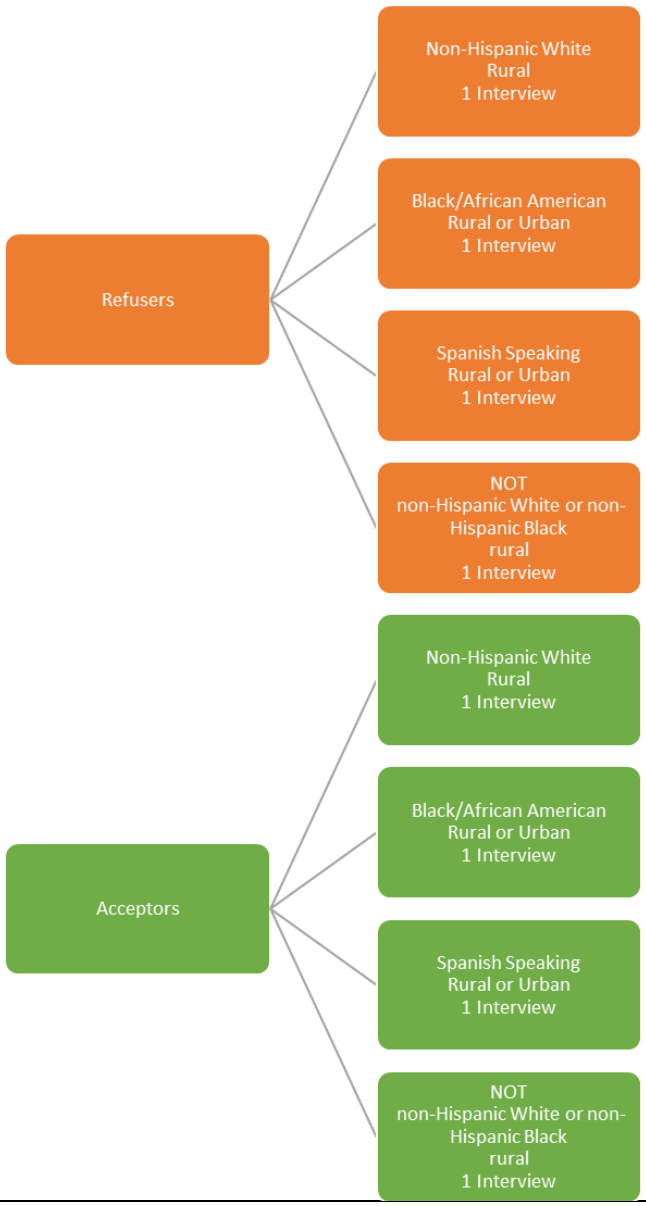

Figure 2. Number of key informant interviews. The study team will host 1 interview per race/ethnic group for the refusers and acceptors.

Key Informant Interviews. The study team will conduct key informant interviews with participants who identify on the pre-interview survey as "vaccine acceptors" and "vaccine refusers." The study team will conduct approximately 1 interview per race/ethnicity strata (Fig. 2) for the vaccine acceptors and vaccine refusers, for a total of approximately 8 interviews (see table below). The study team will maintain wait lists for participants who cannot confirm attendance or no-show participants. If time

constraints prohibit completing all 8 interviews, the study team will conduct the minimal acceptable interviews. The rationale for interviewing these participants individually, rather than in a focus group, is manifold:

1. the study team requires less data from participants who have already fully decided on vaccinating their children since the eventual mHealth app will primarily target participants who are undecided about vaccination;
2. the study team aims to avoid spreading COVID-19 vaccine myths, misinformation, or negative attitudes that vaccine refusers may express;
3. the study team anticipates it will be faster to collect data from vaccine refusers/acceptors participants via individual interviews than to assemble two additional, heterogeneous focus groups.

The key informant interviews will underscore both phrasing and approaches to avoid in the mHealth app, as identified with the vaccine refuser participants, and approaches to highlight as identified with the vaccine acceptor participants.

See the key informant interview guide for possible questions and probes. Actual questions for each interview may vary depending on the flow of conversation and questions may evolve over the course of the study according to the findings of ongoing constructivist grounded theory.

Rescheduling

The study team will reschedule focus groups or key informant interviews if technical difficulties occur or if a quorum of participants is not present. The site research coordinator or designee will contact participants to reschedule focus groups or key informant interviews.

Payment to Research Participants

Participants will receive $50 for focus group participation (approximately 1-hour duration) and $30 for key informant interview participation (approximately 30-minutes duration). Payment to each participant can be monetary, according to institutional policies, or a monetary equivalent of materials (e.g., blankets, sweatshirts, bags, etc.).

Quality Assurance

Key informant interviewers and focus group facilitators will use discussion guides developed by nationally recognized linguistic experts. The DCOC will use a certified translation service to translate these discussion guides to Spanish for Spanish-speaking participants. A research team member skilled

in interview and focus group conduct will meet with interviewers and focus group moderators to confirm past training, review expectations or remediate as needed, and conduct mock session(s) to verify skills. Experienced, qualified, and trained study personnel will train any new focus group moderators,[39] conduct key informant interviews, and focus groups. At least one interviewer and moderator will be fluent in Spanish.

Data Analysis

Data Coding and Analysis

Individual and focus group interviews will be analyzed using textinspector (textinspector.com), Wmatrix (http://ucrel.lancs.ac.uk/wmatrix/), or similar software. Only members of the study team will have access to the recordings for transcribing, coding, interpreting, and analyzing.

The study team will import the transcripts of the focus groups and interviews into textinspector, Wmatrix, or similar software. A constant comparative method will be used to assign codes, categories, and themes during the analysis to reveal perceptions of facilitators and barriers to parental vaccine acceptance and needs for educational purposes, in keeping with grounded theory analytic procedures.[40]

The study team will conduct line-by-line analysis to identify codes that look for actions and meanings, and the team will group these by similarities and differences, based on the conventions of constructivist grounded theory.[41] Other means of coding to generate codes for theme assignment include linguistic cues of causal relations (*because, since),* conditional relations (*if, rather, instead*), taxonomies (lists, pronouncements *X is an...),* time-oriented relations (*next, then),* attributions, contingent relations (*if/then),* and spatial relations (*place, size).* Two study team members, trained in linguistics, will code using consensus agreement. Analysis will stop when emerging patterns of response are saturated and repeated. As a contingency, we will recruit additional participants for either focus groups or key informant interviews if thematic saturation is not reached. Typically, this coding process involves asking analytical questions, coding in gerunds to capture presumptive actions, and comparing data and codes, followed by memo writing to identify categories.[42] Categories will be reviewed to assess emerging theoretic and thematic concepts of explanation and a theory of parental response for each group (accepting, hesitant, refusing). The study team will view the resulting themes to develop intervention priorities for each of the targeted populations, areas of needed information, attitudes for reinforcement and re-framing, necessary skill sets, and institutional barriers requiring more than education.

Risks and Benefits

A risk to study participants is the potential for loss of confidentiality of study data. The study team will take measures to protect the confidentiality of study data, as described in the Data Handling and Recordkeeping section below. Additionally, participants may experience some discomfort or embarrassment during the focus group discussions. Focus group facilitators will work to minimize discomfort during the conversation as much as possible.

Participants may gain knowledge from the study in the focus group discussions and from the follow-up materials from the CDC and AAP. Additionally, knowledge gained from this study could potentially benefit patients in the future.

Data Handling and Recordkeeping

The principal investigator or qualified designee will carefully monitor study procedures to protect the safety of research participants, the quality of the data, and the integrity of the study.

The DCOC will assign each participant a code; however, this code will not be used when transcribing the focus group or interview recordings. The transcriptions will use a de-identification method (e.g., participant 1, participant 2, etc.) not associated with the participant code. The DCOC will manage the key that links the code to the participant identifiers, and the DCOC will store the key in a secure HIPAA-compliant system (e.g., UAMS box), with limited access to specific research staff, namely the operational PI, the director of research, and others as specified by the operational PI. The key to the code will not be destroyed after data have been generated and will be retained for long-term storage at the DCOC.

Site Responsibilities

Data collection is the responsibility of the study staff at the individual ISPCTN site under the supervision of the site investigator. The site investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents must be completed using standard good documentation practices (i.e., the ALCOA-C method [attributable, legible, contemporaneous, original, accurate and complete]). For this study, the expected source documentation would be the potential participant list, video/voice recordings, and transcripts. Throughout the course of the study, all sites will retain the potential participant list and any other source documents in a secure location

according to their local policies and procedures for compliance with HIPAA and human subjects' research. Records will include direct identifiers to all participants. Records will be maintained until at least study close-out and publication. Because we are asking the participants to consent to be contacted for future research, the study team will keep contact information of the participants that agreed to be contacted for future research indefinitely. Records will be retained longer if mandated by the DCOC, NIH, or local and/or state policies and procedures.

Participants or site research coordinators/designees will directly enter their screening data into the REDCap database, as described above. This system complies with HIPAA regulations, provided by the DCOC at University of Arkansas for Medical Sciences (UAMS). The EDC system will include password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

Key Informant and Focus Group Interviews

Focus group leaders and key informant interviewers will record focus groups and interviews on a secure videoconferencing platform (e.g., Zoom or similar platform). Computers (including laptops) used to conduct the virtual interviews and for temporary storage of interview recordings and transcripts will be secured and managed by the interviewer's institutional IT organization in accordance with applicable regulations and institutional requirements for storage of electronic research data. At a minimum, these devices will have whole disk encryption, be joined to a private institutionally managed network, and be supported by the institution's central IT organization. Data will only be temporarily stored on the hard drives of these computers. As soon as possible, after each focus group and interview, focus group leaders/interviewers will upload audio, video, and chat recorded files and auto-transcripts to a shared HIPAA-compliant system (e.g., UAMS Box), managed by DCOC with access limited to key study personnel. Once UAMS confirms the successful upload to the HIPAA compliant system, the focus group/interview leaders or study team member will delete all recordings and transcripts from their computers.

Members of the study team involved in data cleaning, verification, coding, and analysis will access the recordings and transcripts via the shared HIPAA-compliant system (e.g., limited access UAMS Box folder managed by DCOC). The first step will be to de-identify interview and focus group participants in the process of cleaning and verifying the transcripts, prior to data coding and analysis. De-identification will not include participants study identification number or any information that could connect the data to participants. Members of the study team may temporarily download transcripts to their secure

computers, if needed, for these activities. Their devices will adhere to the same safety standards as those used for interviews.

After the study team analyzes the transcripts, they will upload the results to a UAMS limited-access shared Box folder managed by DCOC.

DCOC Responsibilities

The study team will place participant's de-identified data and other limited information, such as race and ethnic group, into a UAMS limited-access shared Box folder or REDCap project that is managed by the DCOC. The study team will share this data in compliance with the NIH data sharing policy.

For future studies using any procedures or analysis not specified in this protocol, IRB approval is required. In the event that another investigator/collaborator has a meaningful purpose for accessing the data retrieved in this protocol, the DCOC must consult the study principal investigators, and the IRB must approve.

Pre-Interview Survey

The DCOC will analyze the pre-interview survey results and stratify respondents as described in the Pre-Interview Survey subsection. The stratified participants will then be grouped by race/ethnicity, as described in the Focus Group subsection of the Interview Procedures subsection. The DCOC will form focus groups or key informant interviews based on common available times among participants. Site research teams will securely access the contact information for participants in these groups and schedule focus groups or key informant interviews. The DCOC will grant limited access to a shared HIPAA-compliant system where the contact information of participants will be stored.

In summary the DCOC will be responsible of the following:

- Creating the REDCap pre-interview survey for data collection. If needed, other similar EDC systems could be used;
- Receiving the pre-interview survey results and generating a list of eligible participants. The list will be stored in a shared limited-access, HIPAA-compliant system. Only research team members will be able to access to it.
- Generating and sharing with the focus group and interview leaders a shared limited-access HIPAA-compliant system where they can upload recordings of the focus groups and individual interviews.

- De-identifying focus groups and key informant interview transcripts. Jessica Snowden, MD, (or current Operational Principal Investigator) will verify that all transcripts are properly de-identified before releasing transcripts for analysis.
- After de-identification, transcription of the recording and analysis, the data will be stored (long-term retention) in a UAMS HIPAA-compliant system managed by DCOC.
- DCOC will manage the list of participants that agreed to be contacted for future research. This list will have limited access.
- DCOC will train the enrolling sites to destroy (from the research records) the contact information of parents/caregivers that decline to participate in the pre-interview survey.

Specimen Handling and Storage

Not applicable

Multisite Research

The UAMS IRB will be the IRB of record for this multisite study. The DCOC will submit the protocol and all participant materials to the central Institutional Review Board (cIRB) for review and approval. ECHO ISPCTN site awardees must use the cIRB-approved protocol and other cIRB-approved participant materials. The cIRB must approve any amendment to the protocol before site awardees implement changes to the trial. Any participant-facing materials must be cIRB approved before a site may use them, and all changes to all participant-facing materials must be cIRB approved. Sites will not share data.

Ethical Considerations

This study is minimal risk, with the primary risk being loss of confidentiality. Risks will be minimized using standard procedures for handling protected health information.

The study team will conduct this study in accordance with all applicable government regulations and University of Arkansas for Medical Sciences research policies and procedures. This protocol and any amendments will be submitted and approved by the IRB as required.

Informed Consent Process

See Enrollment and Informed Consent subsection.

Participant Compensation

See General Procedures subsection of Interview Procedures subsection.

Dissemination of Data

The study team will conduct this study in accordance with the following publication and data sharing policies and regulations:

NIH Public Access Policy

The NIH Public Access Policy ensures that the public has access to the published results of NIH-funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

ECHO ISPCTN Publications and Presentations Policy

This policy ensures accurate, responsible, and efficient communication of findings from ECHO ISPCTN clinical trials. The ECHO ISPCTN Steering Committee has approved and ratified the ECHO ISPCTN Publications and Presentations Policy, which includes representatives from all site awardees, as well as representatives from the NIH and the DCOC.

NIH Data Sharing Policy

We will make every attempt to publish results in peer-reviewed journals. Other researchers may request data from this study by contacting Jeannette Lee, PhD, at the DCOC (or the current Co-Principal Investigator at the DCOC).

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