Official Title: VISTA:Vaccinator-Initiated Screening and TAilored counseling for reducing vaccine hesitancy

NCT#: NCT04421586

Document Date: 11/02/2021

NCT04421586

Purpose of the Study

The purpose is to test the central hypothesis of this study that reducing vaccine hesitancy concerns in pregnant women using VISTA will increase timely uptake of routine vaccinations in their children.

Background & Significance

Globally each year, vaccinations avert 2.5 million childhood deaths, but the World Health Organization (WHO) estimates that a staggering 19.4 million children currently remain under- or unvaccinated.1,2 While access to vaccines in most low- and middle-income countries (LMICs) has been dramatically improved through routine immunization programs, vaccination uptake is often limited by parents' refusal or delay in accepting vaccines for their children – a phenomenon known as vaccine hesitancy.3-7 The WHO estimates that, due to rising rates of vaccine hesitancy globally, there is a critical unmet need for interventions to systematically address this public health dilemma.3-5,8-10 However, addressing vaccine hesitancy faces three bottlenecks: (1) screening for hesitancy concerns is not integrated within routine maternal or child health services, (2) most existing interventions provide vaccination facts but are not tailored to target individuals' hesitancy concerns, or culturally-adapted to their setting, potentially limiting effectiveness, and there is a weak evidence-base on effectiveness of strategies to mitigate hesitancy.9,11 To overcome these bottlenecks, the overall objective of this study is to develop and evaluate VISTA – a vaccinator-initiated screening and tailored counseling intervention for reducing vaccine hesitancy.

According to the 2015-16 Demographic and Health Survey, 1 in 4 Tanzanian children fail to receive all vaccinations recommended in the first year of life [1]. Access to health facilities in rural areas only partly explains this suboptimal coverage, and further research is needed to understand the reasons parents are unable or choose not to vaccinate their child (e.g., due to vaccine hesitancy). Most research on vaccine hesitancy to date has been centered in North America and Europe, with few studies from LMICs, despite vaccine hesitancy's global presence.3,9,11,12 Duke and NIMR have previously collaborated on an NIH-funded R21 study (1R21TW010262) in Tanzania to evaluate efficacy of mobile phone-assisted conditional cash transfers in reducing barriers to vaccination, such as transportation. In this study, we used a 10-point scale to measure vaccine hesitancy concerns in a cohort of 133 mothers. We found that 86% of rural mothers and 76% of urban mothers had at least one hesitancy concern. Moreover, 30% of mothers had three or more concerns, with the biggest concern being administration of multiple vaccines in a single clinical visit.

Since routine childhood vaccinations are due starting at birth, we propose to develop VISTA for pregnant women, allowing vaccine hesitancy to be systematically identified and mitigated before the child's birth. Using a health provider-initiated approach is advantageous for two reasons: Majority (98.5%) of mothers in the R21 study noted the health provider as their primary and most trusted source of health information, and in most government health facilities in Tanzania, the same provider is responsible for provision of ANC, delivery, and childhood vaccinations services. Community health workers and other lay health workers could serve as alternatives to or as supportive aids to health providers as they are trusted resources in the communities and can educate women in homes or communities.

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Design & Procedures

The study will be primarily undertaken in Mtwara region with some activities (e.g., stakeholder interviews, pilot testing etc) occurring in and surrounding areas of Dar-es-Salaam and Dodoma.

Study intervention

VISTA will comprise two components: (1) A screening tool, which allows identification of hesitant women and their specific concerns, and (2) A counseling script that incorporates education about vaccinations and its benefits (core messages), as well as content targeted to individually-specific vaccine hesitancy concerns (tailored messages). Women receiving VISTA will, hence, get the same core messages but differing tailored messages depending on their hesitancy concerns. The VISTA intervention components will be optimized for cultural appropriateness of content, implementation feasibility, and integration with existing antenatal care services in Tanzania.

Procedures by aim

Aim 1. Develop and adapt VISTA using stakeholder input to improve cultural appropriateness of content, implementation feasibility, and integration with existing ANC services in Tanzania.

A. VISTA screening tool: The 10-point hesitancy scale (Box 1) based partly on the WHO survey is being tested further for relevance with a newly enrolled cohort of 400 pregnant women in an ongoing R21 study. Focus group data on barriers to timely vaccination are also available from the R21 study. Using these data, we will edit scale items to reflect hesitancy concerns of Tanzanian women. The updated scale will be used as VISTA's screening tool after translation to Kiswahili, and refinement in C below.

Box 1: 10-Item vaccine hesitancy scale.

(Answer choices were agree, disagree, or unsure)

1. Vaccinations can prevent deadly diseases.
2. One dose of vaccine is enough. Multiple doses are not required.
3. It is safe for a child to receive multiple vaccines in one appointment.

4. My child does not need vaccines for diseases that are not common anymore.
5. Children who are healthy do not need vaccinations.
6. Some babies are too small to get vaccines -- it is better to wait until they are older.
7. I am concerned about the side effects of vaccines.
8. The benefits of vaccines outweigh the minor side effects like low-grade fever, fussiness, or soreness at the site of the injection.
9. Vaccines work only if given before the disease strikes.
10. Having my child vaccinated is important for the health of others in my community.

B. VISTA counseling content: Educational content on vaccinations will be referenced from three primary sources in the development of VISTA counseling scripts – (1) US Centers for Disease Control information sheets on vaccines, (2) Baby Center frequently asked questions and vaccination basics, and (3) the 10 facts about immunizations at WHO.. In addition, Immunization and Vaccines Development (IVD) Program and the Mtwara Regional Medical Office will be contacted for any Tanzania-specific guidelines and content. Once appropriate content is identified, it will be adapted into a counseling script comprising of core and "tailored" messages (1/concern, a few sentences each), and translated to Kiswahili. Feedback on these a-priori scripts will be obtained in C. below

C. Refining cultural-appropriateness and health system integration: Qualitative interviews with pregnant women (n=20), health providers (n=10), and stakeholders (n=10, e.g., regional and district vaccine officers, village leaders) will be used to elicit feedback on VISTA content, comprehension, acceptability, and cultural appropriateness. Interviews will preferably be conducted individually. However, if participants are in the same location (e.g., government officials working in the same office), we may group participants (2-3 per interview) for efficiency. Health provider and stakeholder interviews will also examine opportunities for integration of VISTA with routine ANC services. Interviews will be conducted in Kiswahili, audio-recorded, transcribed, and translated to English for further review. Feedback will be documented using Bernal's framework of intervention dimensions (language, persons, metaphors, content, concepts, goals, methods, and context) and inform iterations of VISTA. Intervention adaptation will be supervised by an expert review panel comprising of Tanzanian stakeholders (Leadership from NIMR, IVD, and the Mtwara Regional Medical Office).

Aim 2: Evaluate the intervention fidelity and preliminary efficacy of VISTA for reducing parental vaccine hesitancy and improving vaccination uptake in children, compared to usual care in Tanzania.

For this aim, 10 study sites will be initially selected and non-randomly assigned to receive VISTA or usual care (see Figure 1). Study sites will comprise rural health facilities and their surrounding communities in Mtwara, Tanzania. If enrollment targets are not met (e.g., due to lower than expected pregnancy rates), we will include up to 10 additional study sites.

For this study, we will define health workers as facility-based workers as well as community-based workers (e.g., community health workers or other lay health workers). Up to 10 health workers from each intervention site will be enrolled in the study and participate in a 1-day training workshop. Training
topics will include national vaccination guidelines, vaccine hesitancy, and VISTA tools. During the training, we may incorporate interactives activities such as health workers practicing using VISTA through role-playing and observing peers use VISTA. Peer-feedback on content coverage, delivery, and areas for improvement will be discussed in any interactive activities. Post-training, these health workers will implement VISTA in the intervention sites. Observations, surveys and interviews with health workers will examine acceptability of VISTA, challenges with implementation and feedback for improvement of content, comprehension and so forth.

Approximately 20 women will pilot the Baseline or Follow-up surveys. Study staff will solicit women's feedback.

Approximately 60 third trimester pregnant women with at least one hesitancy concern when screened by study staff using the VISTA screening tool will be offered participation in the study (30 intervention, 30 control). Consenting women will participate in a baseline survey. Women will be asked to provide a birth notification within 2 weeks of delivery, or a

study member may follow up to record birth outcomes. A follow-up survey will be conducted (in person or by phone) approximately 4-6 months after the birth to capture vaccine uptake and timeliness for the child.

STUDY OUTCOMES ARE SUMMARIZED IN TABLE 1.

ABLE 1: Study outcomes			
Outcomes	**Data source and method**	**Description**	**Timeframe**
Primary			
Reduction of concerns (primary, intervention arm only)	VISTA screening tool completed by study staff during eligibility screening, and baseline survey (VISTA screening tool repeated).	• Percentage of women with reduced number of concerns immediately post-counseling in the intervention arm.	Pre-counseling; post-counseling (Baseline)
Secondary			
Hesitancy concern risk ratio (intervention and control arms)	VISTA screening tool completed at eligibility screening and follow-up survey	• Percentage of women with reduced number of concerns in intervention versus control arm	Follow up (up to 6-months post birth)
Timely vaccination (intervention and control arms)	Dates of vaccinations from government-issued vaccination cards. Calculated as a vaccination (event=1) that occurred within a 4-week window of due date.	• Percentage of children by vaccine who received the vaccine within 4-week window of due date in intervention versus control arm	Follow up (up to 6-months post birth)
Days unvaccinated (intervention and control arms)	Dates of vaccinations from government-issued vaccination cards. Continuous outcome, for each vaccine.	• Mean number of days children remain unvaccinated for each vaccine in intervention versus control arm • Median number of days children remain unvaccinated for each vaccine in intervention versus control arm	Follow up (up to 6-months post birth)
Fidelity (intervention only)	Observation of provider-patient interactions by study staff. Measured as part of a fidelity checklist.	• Percentage of checklist items completed during counseling in intervention arm. • Feedback recorded on implementation of screening tool, delivery and coverage of counseling content. • Mean number of minutes spent delivering counseling per woman in intervention arm.	Baseline (during counseling)
Acceptability (intervention only)	Baseline survey with women	(For women): • Percentage of women in the intervention arm who say that	Baseline (post-counseling)

		the information provided by the CHW is helpful • Percentage of women in the intervention arm who say that the information provided by the CHW reduced their concerns about vaccinations • Percentage of women in the intervention arm who say that the CHW helped them understand why children needed vaccines • Percentage of women in the intervention arm who say that the CHW answered most of their questions • Percentage of women in the intervention arm who say that the CHW was respectful • Percentage of women in the intervention arm who say that the CHW explained things in terms they could understand • Percentage of women in the intervention arm who were satisfied with their conversation with the CHW • Percentage of women in the intervention arm who say they are comfortable vaccinating their child • Percentage of women in the intervention arm who say they will speak with the CHW again • Percentage of women in the intervention arm who say they would refer the CHW to their friends and family	

Selection of Subjects

There are four groups of participants in the study:

1. Individuals approached to participate in intervention development will be pregnant women (n=20), health providers (n=10), and stakeholders (n=10, e.g., regional and district vaccine officers, village leaders etc.).
   - Health providers will be selected in consultation with the Regional and District Medical Administration of Mtwara, and may overlap with providers selected to participate in the implementation of intervention.
   - Stakeholders will be selected in consultation with the local PI to reflect expertise in National and Regional Immunization policies, medical administration, as well as community leadership in Mtwara.
   - Finally, 20 third trimester pregnant women will be selected purposively from rural health facilities in Mtwara.

2. Approximately 20 women will be enrolled to participate in pilot testing of surveys. To be eligible, women must be:
   - Pregnant and/or a mother of at least one child 5 years old or younger
   - At least 18 years of age

- Attend a health facility that has been selected for pilot testing. Health facilities will be chosen in consultation with the local PI, Dr. Mfinanga, and located in or around Dar es Salaam.

3. For the VISTA evaluation, up to 10 health facilities will be selected using data and experiences from a prior R21 study in Mtwara, and in consultation and/or input from stakeholders. Up to ten additional sites will be added if recruitment targets are not met. Study sites will be non-randomly assigned to receive VISTA or usual care.
   - Up to 10 health workers (including community health workers (CHW) from each of intervention site will participate in the study. Health workers must be:
   - 18 years of age or older
   - Associated with one of the intervention health facilities

4. Approximately 60 women will be enrolled for the VISTA evaluation (30 intervention; 30 control). To be eligible, women must be:
   - In the third trimester of pregnancy
   - Residing in a study site (intervention or control)
   - At least 15 years of age
   - Planning to reside in the study site for the duration of their participation in the study (until approximately 6 months after delivery to enable follow up).
   - Have at least 1 concern about childhood vaccines

During the consent process, we will include statements that explain that, once the child is born, study staff will collect information regarding this child health and vaccinations. The consent will also mention that in case the participant is not present (e.g. maternal death, moved) we will get birth outcome information collected from a family member, friend or community leader.

Subject Recruitment and Compensation

This study does not include Duke University Health System (DUHS) patients.

Study staff will approach pregnant women in study sites in Mtwara, Tanzania, to screen for eligibility. Eligible women will be offered enrollment. Only those women providing informed consent will be included in the study. Due to the focus of VISTA evaluation on childhood vaccinations, study enrollment is limited to pregnant women in their third trimester. Any eligible pregnant woman will be offered enrollment until the enrollment targets are met.

In consultation with the Regional and District Medical Administration of Mtwara, health workers working in study facilities and surrounding communities will be recruited to participate in the study.

Other experts and stakeholders participating in intervention development will be purposively selected in consultation with the local PI, Dr. Mfinanga.

In consultation with the local PI, Dr. Mfinanga, and staff of health facilities near Dar es Salaam, research staff will identify pregnant women, or mothers of children 5 years or younger who attends health facilities selected for pilot testing.

As part of our recruitment and retention strategies, we will interface with balozis and other community-based leaders. Therefore, we will collect their contact information in order to reach out to them over the course of the study. They will help with retention of women for the follow-up data collection. In the consent, we will inform women that their study participation may be shared with balozis and other community-based leaders, if research staff need assistance in finding them for the follow-up data collection. The consent will also indicate that, the event women are not available for follow-up, study staff may contact a family member, friend, or community member to obtain birth outcome information. Therefore, their contact information will also be collected.

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Study compensation

(Compensation amounts are based on Tanzanian input. Following Tanzanian guidelines. Payments should usually not be more than travelling expenses and/or loss of earnings and must not be coercive or represent an undue inducement to take part).

Participants will be compensated in Tanzanian Shillings (TSH).

Women piloting the baseline and/or follow-up survey will be compensated:

- TSH 7,500 (approximately $3 US) for baseline
- TSH 7,500 (approximately $3 US) for follow-up

Pregnant women will be compensated:

- TSH 7,500 (approximately $3 US) for baseline
- TSH 2,500 (approximately $1 US) for birth notification
- TSH 7,500 (approximately $3 US) for follow-up

Health workers will receive the regional government per diem of up to TSH 80,000 (approx. $35 US).

Subject's Capacity to Give Legally Effective Consent

Participants will only be included if they have the capacity to give legally effective consent.

Pregnant women who are aged 18 years or older can consent for themselves.

For those pregnant women who are under 18 and have never married, we will seek assent from the women, and written informed consent from a parent, guardian, or local community leader.

Pregnant women who are under 18 years, and who are married or have previously been married, will be allowed to consent for themselves to participate in research due to the reasons listed below. The age of majority for young pregnant women is determined by Tanzanian law as interpreted by the Tanzanian IRB

According to the Tanzania Demographics and Health Survey, 27% of women ages 15-19 years have had either a birth or are pregnant. Since excluding women under 18 will exclude this key population of often first time mothers, this study would like to include pregnant women who are 15+.

A waiver of parental consent is requested for pregnant women 15-17 years old who are married or were previously married. In Tanzania, adolescents under age 18 who are sexually active have the right to access reproductive health services without parental or spousal consent and they can make associated medical decisions on their own behalf. Given that sexually active adolescents have this "adult" right to medical decision-making, we posit that sexually active adolescents, including young mothers under the age of 18 are also able to consent to research participation for themselves without parental or spousal consent.

The study intervention is a counseling intervention, which seeks to provide evidence-based information on vaccinations. Risks from participation in this study are judged to be minimal.

Since pregnant women will be approached for study participation at governmental health facilities or in their homes or communities during working hours, it would require significant resources (personnel and financial) to trace parents/spouses of eligible women in rural communities, which are often geographically distant from health facilities. Hence, we request that the additional step of getting parental, guardian or community leader consent be conducted only for vulnerable women (under 18, pregnant, and never married).

Risk/Benefit Assessment

Potential risks from participation in the study:

- Risks from participation in this study are minimal and commensurate with normal life. In addition, since the intervention being tested is educational in nature, no adverse events are expected. Women's receipt of antenatal care or follow on health services will not be impacted if they choose to decline study participation.
- There is a potential risk of loss of confidentiality. Steps will be taken to minimize loss of confidentiality by using secure systems to store data, limiting access to study data to only authorized individuals, and by storing identifying information (e.g., on consent forms, enrollment logs, contact details, etc.) separately from survey responses. Identifiable information in semi-structured interview transcripts will be redacted.

Potential benefits from participation in the study:

- If the intervention is successful in reducing parental concerns towards vaccines, it may lead to more timely vaccination of the child, and subsequently, potentially reduced morbidity and/or mortality due to vaccine-preventable illnesses.
- The knowledge gained from the research will help us better understand:
- How to screen for parental concerns related to vaccines
- How to counsel parents to reduce vaccine-related concerns
- The impact of screening and counseling pregnant women on timely vaccination status of their children.

Costs to the Subject

There are no costs to the participants for participating in the study.

Data Analysis & Statistical Considerations

Aim 1: VISTA development

Qualitative interviews use a purposive sampling approach. Interviews will be conducted in Kiswahili, audio- recorded, transcribed, and translated to English for further review. Feedback will be documented using Bernal's framework of intervention dimensions (language, persons, metaphors, content, concepts, goals, methods, and context) and inform iterations of VISTA. Intervention adaptation will be supervised by an expert review panel comprising of Duke University investigators and Tanzanian stakeholders (Leadership from NIMR, IVD, and the Mtwara Regional Medical Office).

For VISTA development: Sample size for qualitative interviews is based on recommendations by Namey et al., to be able to achieve saturation of themes. According to these studies, for qualitative interviews, 88% saturation of themes can be achieved with a sample of 6-12 interviews. Our proposed sample size is in this range.

Aim 2: VISTA pilot evaluation

Sample size calculations: We plan to enroll approximately 60pregnant women for the evaluation study and, if feasible, we will enroll equal numbers into each arm (30per arm, intervention and control). The high total fertility rate in Tanzania (5.2 children/woman), and previous experience recruiting 400 pregnant women in Mtwara for the R21 study, suggest recruitment of 60 women to be feasible in this study's timeline. The sample size is based on a convenience sample, and the study is not powered to detect a meaningful/statistically significant change in effect. Instead, the sample size is chosen to provide information on study feasibility, fidelity of intervention delivery, and factors (positively or negatively) affecting implementation. Data from this study will inform a fully powered evaluation of the VISTA intervention in the future.

Data analysis: Baseline socio-demographic variables will be summarized using descriptive statistics in addition to data on intervention feasibility, acceptability and fidelity. Outcome measures will be analyzed as described in Table 1. A modified poisson regression model with robust standard errors will be fitted to resulting data. Model parameters for time (pre-/post-), intervention arm, and interaction effect of time and intervention arm will be estimated. Interpretation will focus on the interaction term, which estimates change in the proportion from baseline, comparing the two arms.

Data & Safety Monitoring

There are no adverse events anticipated from participation in the study.

The study proposes an educational intervention to promote positive vaccination behavior. In this intervention, health providers will systematically provide counseling to third trimester pregnant women about vaccines that their child should receive after birth. The study poses no more than minimal risk to the participants since the intervention is educational in nature, and not invasive.

The investigators will make all study related documents, including consent forms, readily available for inspection by the study's IRBs, NIMR and its authorized site monitors and the Office for Human Research Protection (OHRP). On-site study monitoring will be performed by the study and local PIs or their designees, to verify compliance with human subjects and other research regulations and guidelines, assess adherence to the study protocol, and confirm the quality and accuracy of information collected and entered into the study database. The study will be conducted in full compliance with the protocol. With the exception of modifications required to eliminate immediate participant safety concerns, the protocol will not be amended without approval from the study PI.