Leading Advancements in the Uptake of Newborn Community Health (LAUNCH) Trial Protocol

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Summary:

Background: One in every 15 Ethiopian children die before their fifth birthday and 7 in 10 of those deaths occur during infancy. Optimizing nutrition in young infants is one of the most effective interventions to improve infant survival and growth. In Ethiopia, only 7% of children age 6-23 months meet the minimum acceptable dietary standards and, in the Amhara region where this intervention will take place, only 3% of children under two years old get the minimum dietary diversity they need for healthy growth and development. The Amhara region is characterized by its religious tradition with 84% of the population belonging to the Ethiopian Orthodox faith tradition. Partnerships with faith leaders may provide a culturally relevant platform for accessing women and infants, increasing uptake of practices known to improve infant health and development, and providing support for women in the postnatal period and throughout the first year of their child's life.

Objective: The study aims to determine the impact of a behavior change intervention that partners Orthodox priests with members of the Health Development Army (HDA) and trains them to conduct newborn health outreach to increase rates of early initiation of exclusive breastfeeding through 6 months and vaccination coverage at six months. We will also determine the impact of the intervention on infant growth at between 5 and 6 months of age, observed and self-reported changes in nutrition and feeding practices of mother and infants, and early identification of newborn illness.

Methods: The study utilizes a community-randomized trial design in which 11 communities will be randomized to receive the intervention and 11 communities will be randomized as control communities. The unit of randomization at the house of worship. The target population for this undertaking is pregnant women and women who recently delivered in rural communities in the North Gondar region of Ethiopia. Infants enrolled in the study will have a baseline evaluation within 10 days of birth and the primary outcomes of mid-upper arm circumference (MUAC) and exclusive breastfeeding will be measured at a follow-up visit at between 5 and 6 months after birth. The sample size of 150 infants from intervention churches and 150 infants from control churches is based on identifying a statistically significant difference of ≥0.2 cm in mid-upper arm circumference (MUAC) with 80% power at α=0.05, anticipating 20% of participants being lost to follow-up. We will also have 80% power to detect a significant difference of 50% exclusive breastfeeding at 5-months in the control group versus 70% in the intervention group.

Introduction:

The need for improving newborn and infant health and the behaviors that contribute to outcomes in Ethiopia is clear. One in every 17 Ethiopian children die before their fifth birthday and 7 in 10 of those deaths occur during infancy. Causes for newborn mortality are not always well documented, but literature suggests that prematurity, asphyxia, and infection are leading causes of newborn and infant death.[1][2] Infections in newborns remain a large threat to newborn survival in Ethiopia. Acute infections causing pneumonia, fever, and diarrheal disease contribute substantially to the burden (over 31%) of under five deaths, and less than half of children with reported symptoms sought any care or treatment according to recent estimates.[3]

While both child and infant mortality rates have dropped substantially over the past 15 years, progress in reducing newborn deaths has been slower[4] pointing to challenges and complexities in changing behaviors and practices around identifying illness and delivering newborn care. For children who do survive, poor nutrition and its impacts on growth and development are widely observed. Seven percent of children in Ethiopia suffer from acute malnutrition (wasting). Perhaps more importantly, in Ethiopia, 37% of children under five in Ethiopia are stunted, or below their expected height for age, a sign of chronic undernutrition. Stunting is associated with significantly higher rates of mortality, with cognitive and developmental delays and with lower income earning potential. Ultimately, stunting is a critical driver of poor economic development in many low-income settings. This clearly represents an important intervention opportunity to improve survival, development, and productivity.

Optimizing nutrition in young infants is one of the most effective interventions to improve infant survival and growth. In Ethiopia, only 14% of children age 6-23 months meet the minimum acceptable dietary standards and, in the Amhara region where SCOPE works, only 7% of children under two years old get the minimum dietary diversity they need for healthy growth and development.[5] Exclusive breastfeeding in the first six months of life has the potential to dramatically improve growth and survival. However, cultural and social pressures often result in cessation of exclusive breastfeeding at younger ages, with significant impacts on future growth and development.

Healthcare providers have limited interactions with women when they leave a health facility after birth. While home visitation is nominally a pillar of postnatal care, logistical challenges to follow-up and systematic implementation of home visits remains challenging in Ethiopia, where only 34% of women with registered births receive any postnatal care. In addition, only half (48%) give birth in a health facility and

[1] Mengesha, H. G., &Sahle, B. W. (2017). Cause of neonatal deaths in Northern Ethiopia: a prospective cohort study. BMC Public Health, 17, 62. http://doi.org/10.1186/s12889-016-3979-8

[2] BerheWeldearegawi et al. BMC Public Health201515:770 https://doi.org/10.1186/s12889-015-2090-x 11 August 2015.

[3] Central Statistical Agency - CSA/Ethiopia and ICF. 2019. Ethiopia Demographic and Health Survey 2019. Addis Ababa, Ethiopia: CSA and ICF. Available at https://dhsprogram.com/pubs/pdf/FR363/FR363.pdf

[4] Central Statistical Agency - CSA/Ethiopia and ICF. 2019. Ethiopia Demographic and Health Survey 2019. Addis Ababa, Ethiopia: CSA and ICF. Available at https://dhsprogram.com/pubs/pdf/FR363/FR363.pdf.

[5] Central Statistical Agency - CSA/Ethiopia and ICF. 2019. Ethiopia Demographic and Health Survey 2019. Addis Ababa, Ethiopia: CSA and ICF. Available at https://dhsprogram.com/pubs/pdf/FR363/FR363.pdf

would be registered for such visits.[6] Several critical elements of essential newborn care and early infant feeding can be practiced at home and in the community including exclusive breastfeeding, kangaroo mother care, feeding, hygiene, and early identification of infections. Partnerships with faith leaders may provide a culturally relevant platform for accessing women and infants, increasing uptake of practices known to improve infant health and development, and providing support for women in the postnatal period and throughout the first year of their child's life.

Study Objectives:

The **primary objective** of the study is to determine the impact of a behavior change intervention that partners Orthodox priests with members of the Health Development Army (HDA) and trains them to conduct newborn health outreach to increase rates of early initiation of and exclusive breastfeeding through 6 months and vaccination coverage at 6 months.

Secondary objectives include:

- Determine the impact of the intervention on infant growth at six months, observed and self-reported changes in nutrition and feeding practices of mother and infants, and early identification of newborn illness.
- Design a culturally relevant, scalable intervention for community-based newborn and infant health in Gondar in partnership with local partners, the Federal Ministry of Health, and the Gondar Regional Health Bureau.

Methods:

Study Design:

In collaboration with the woreda administrative office and the woreda diocese of the EOC, all the kebeles and EOC churches in the woreda will be mapped by the study team and randomly assigned to intervention or control. Sites will be selected in a way that ensures they are reasonably far apart in order to avoid contamination. Newborn-mother pairs in the catchment areas of the intervention churches will receive the intervention, whereas those in the control churches will receive routine community health packages implemented by community health workers (HEWs and HDAs).

The intervention will be implemented at the community level by pairs of trained EOC priests and members of the HDA. A list of priests serving at the EOC churches in the intervention arm will be obtained through the woreda diocese and their respective churches. All the priests will be contacted through the church leadership and asked to participate in the study intervention. The intervention will be implemented in collaboration with HDA members recruited by HEWs under the health centers in the catchment areas of the intervention churches. HDA members 55 years old or younger will be asked to participate.

An initial 5-day training will be given to priests and HDA members. The training will focus on newborn health topics including early initiation of and exclusive breastfeeding, maternal nutrition, immunization, childhood illnesses, child health care services, etc. At the end of the training action plans will be prepared by the training organizers, priests, and HDA. Priest will be asked to integrate health messages

[6] Central Statistical Agency - CSA/Ethiopia and ICF. 2017. Ethiopia Demographic and Health Survey 2016. Addis Ababa, Ethiopia: CSA and ICF. Available at http://dhsprogram.com/pubs/pdf/FR328/FR328.pdf.

and education into their routine family visits around the birth of a child in structured intervals as culturally appropriate.

The trained priests and HDA members will be dispatched to their respective communities to begin the intervention. Their primary activities will be identification of near-term pregnant and newly delivered women, providing health education to their families, follow-up visits to enable newborn-mother pairs to access child health care services, and to provide health education at religious and community gatherings. Specifically, pre-planned visits of parishioners' families will be done by the respective priests and the partnering HDA members during the last month of pregnancy, immediately after the delivery of the baby and around the time of baptism for the newborn. These visits will be used to educate pregnant and postpartum women and their families on newborn health topics including initiation of breastfeeding, duration of breastfeeding/ exclusive breastfeeding, vaccination, cord care, and utilization of available newborn health care services. These community-based activities will be monitored through regular follow-up visits by the UoG study team and discussions with priests and HDA members.

Prospective follow-up

Research assistants will work for the zonal health office to identify all births occurring in the study area. Independent of the intervention outreach teams, the research assistants will attempt to contact all newborn-mother pairs within 10-days of birth. Most contacts will occur at home, but contact may be made at other locations (e.g., health facility, church). Mothers will be invited to participate in the study, and each participating newborn-mother pair will be followed-up by the study team for up to 6 months after enrollment.

Data Collection

The UoG study team will conduct regular visits in both the intervention and control communities to screen, consent, and register new newborn-mother pairs reported by HEWs, collect baseline data from them, arrange follow-up visit schedules, and collect follow-up data from previously enrolled study participants. Each newborn-mother pair will receive up to three visits by the study team in the sixth month period. The study team will use OpenDataKit (ODK), an electronic data collection system to record data on tablets. The study team will upload the collected data to a secured central web-based server upon return to the UoG campus. The overall processes of recruitment and subsequent data collection activities will be supervised by an on-site study manager. The study team will rely heavily on pre-designed standard operating procedures that contain detailed, step-by-step instructions for collecting and handling data.

The following primary and secondary outcome variables will be assessed in this study:

Primary outcome variables*:* mid-upper arm circumference (MUAC), proportion of mothers exclusive breastfeeding

Secondary outcome variables: immunization status (complete vaccination and individual vaccines), frequency of acute illnesses, and frequency of hospitalization

Predictors (other than intervention): maternal age, sex of child, maternal education, family economic status, family size, etc.

Statistical analysis plan

We will compare infant outcomes between children exposed to the intervention and those in control communities. We will use logistic regression to compare dichotomous outcomes (e.g., exclusive breastfeeding through 6 months, completion of vaccinations, infant hospitalization) and linear regression for continuous outcomes (e.g., mid-upper arm circumference). Primary outcomes will be evaluated using an intention-to-treat analysis without adjustment for other covariates. We will account for correlation within church communities by adjusting the variance for the effect of clustering.

Study Participants:

The study includes the following participants:

Newborn-mother pairs in the community reached by the intervention teams (Counseled mothers)

Parishes will be randomized to receive an outreach intervention. Pregnant and postpartum women and their families will be the focus of this outreach conducted at community events, religious services, and in individual home visits by both religious leaders and members of the Health Development Army. Priest and HDA trainees in the study will be trained to discuss the topics of newborn care with pregnant women and their families. Priests and HDA members will offer women and their families an opportunity to decline individual counseling on these topics as part of their scripted protocol.

Newborn-mother pairs approached to enroll in prospective follow-up (Enrolled women and newborns)

The LAUNCH study team will collect individual-level data from each participating newborn-mother pair in the trial to measure exclusive breastfeeding, vaccination coverage, anthropometry, community engagement, and other indicators of maternal and child health.

Inclusion and Exclusion Criteria:

Inclusion Criteria:

Newborn-mother pairs visited by the study staff (Enrolled women and newborns)

The following inclusion criteria will be used during recruitment:

- Newborns should be those delivered at least one month after the start of the intervention period
- Newborn-mother pairs will include only biological mothers
- Newborn-mother pairs should be EOC parishioners
- Newborn's family should have a soul father (a spiritual advisor assigned to the family in the Ethiopian Orthodox tradition)
- Mother must have lived in the study area for at least 6 months
- Mothers must give written informed consent for themselves and their newborn

Exclusion Criteria:

Newborn-mother pairs visited by the study staff (Enrolled women and newborns)

The following exclusion criteria will be used during recruitment:

- Newborns with gross developmental abnormalities that would make anthropometric measurements and interpretations difficult
- Newborn whose mother is not a member of an EOC parish

- Newborns whose mothers have died by the time of recruitment
- Newborn whose family plans to re-locate away from the study site in less than 6 months

Number of Subjects:

Group name/description	Desired number of individuals (or other subject unit) who will complete the research
Newborn/Mother Pairs	240

Procedures:
The intervention in this study is intimately tied to the cultural customs and values of the North Gondar region of Ethiopia. In this region, religious leaders of the Orthodox Church have the potential to be strong advocates or hindrances to effort to improve public health and this study aims to explore how linking religious leaders to frontline health workers may catalyze and empower local communities to improve health outcomes for newborns. The study engages several experienced Ethiopian investigators and will seek continual input from a Steering Committee of community members in Gondar to ensure that all elements of the study are culturally appropriate and conducive to the local context.

Newborn-mother pairs will be recruited within the first 10 days after delivery as reported to the study team by Health Extension Workers (HEWs) engaged in the study. Recruitment will start one month following the start of the intervention and all reported newborn-mother pairs who meet the screening criteria will be included in the study until the calculated sample sizes are reached. HEW's routine registers of new deliveries will be used to trace, recruit and screen study participants. Newborn-mother pairs who fulfill an initial screening criteria will be reported to the study team at the University of Gondar (UoG) who will travel to the study site regularly for recruitment of study participants and data collection. Newborn-mother pairs will be reported to the UoG study team both through phone calls made by HEWs and in-person at the time of regular onsite visits by the team.

Eligible newborn-mother pairs will be visited by a member of the study team at their home or at an appointed meeting location in their community to complete the verbal informed consent process. Those pairs who attend church at a parish that received the intervention will be assigned to the intervention arm, and those from the parishes where no intervention was conducted will be assigned to the control arm. Initial baseline data will then be collected and follow-up visit schedules arranged with the study team.

The following materials will be used during the recruitment of study participants:

- Oral consent scripts (see attached scripts) will be used to provide information about the study to potential subjects.
- A checklist of the initial screening criteria will be used by the HEWs and study team to identify appropriate newborn-mother pairs.

No payment will be provided for participating in the study. Some women may be eligible to receive a travel reimbursement (including transportation and meal stipend) to compensate them for attending scheduled meetings for study follow-up. The maximum value of a travel reimbursement will be $5. In special cases, women travelling longer distances may be compensated to a greater degree on a case by case basis. Non-monetary compensation may include refreshments provided by the study at focus group

discussion, meetings, and gatherings. Participating infant-mother pairs will also have basic anthropometric measurements taken by the study staff free of charge, which some participants may view as a benefit of participation.

Measurement of the impact of the intervention

Data Sources:

Structured questionnaire for newborn-mother pairs
Mothers will be interviewed using an electronic, structured, and pretested questionnaire to collect socio-demographic variables, nutritional history of the mother and newborn, newborn hygiene, history of newborn illness and hospitalization, and exposure to the intervention elements.

Anthropometric measurements of newborns and mothers
Anthropometric measurements of both mothers and newborns will be taken by members of the study team on routine visits using a measuring tape, scale, board and/or other measurement tools.

Immunization cards
Immunization cards will be reviewed by the study team on routine visit to collect data on the newborn's overall immunization completeness.

Consent Process:

Newborn-mother pairs who have been recruited to participate in the study will meet with a member of the study team in a private setting either at home or other private setting. The study team member will read the oral consent script to the potential subject. At the end of the script, the potential subject will be given an opportunity to ask questions about the study procedures and their rights as a research subject. They will be offered a printed copy of the consent script. The study team member conducting the consent process will ask the potential subject some questions related to the voluntary nature of participation to assess their understanding of their rights as a research subject. Any misunderstandings will be clarified. If they are not interested in participating in the research, they will be thanked for their time. Those willing to participate will give their verbal consent and the registration interview will proceed.

We will use research assistants trained in research ethics to initiate all recruitment efforts, which will take place in one-on-one conversations with potential participants. All recruitment conversations will take place with highly trained research staff, using standardized scripts. Once potential participants enroll, all conversations with study personnel will take place in secure, private rooms. We will remind participants that they do not have to answer questions that make them uncomfortable.

The study team member conducting the consent process will ask the potential subject some questions related to the voluntary nature of participation to assess their understanding of their rights as a research subject. Any misunderstandings will be clarified. Upon approval of the English version of the oral consent scripts, they will be translated into Amharic. The translator will be a native Amharic speaker and fluent English speaker with extensive experience in human subjects research. In the event that a participant is unable to read the consent form themselves, the consent form will be read to them out

loud. Participants unable to write their signature will document their consent by placing a thumb print on the consent form.

Involvement of minors:
Biological mothers and their newborn infants will be included in the study.

Assent Process for Minors:
Age of consent for participation in research in Ethiopia is 18 years. However, the National Research Ethics Review Guidelines for Ethiopia section 8.3.5.3 regarding consent for children states: "Emancipated minors- working or earn their living, married, parenting- may be allowed to give an informed consent or an IRB may decide a waiver of consent." Thus, mothers <18 years of age will be included in the study under the standard consent process.

Mothers will provide parental consent for their newborns to participate in the study.

Data Security Protections:

With consent from subjects, we will store questionnaire data, vaccine history data, and anthropometric data.

Study data and contact information will both be collected electronically and stored in separate secure password protected databases. Information in these databases will be linkable by the study ID number assigned to each newborn-infant pair. All analysis and dissemination will involve de-identified data that is referenced by the unique study ID. The link between the study ID and the individual identifiers will be maintained by the lead investigators on University of Gondar study team, who will limit access to only those who need the identifiers to complete their approved study activities.

Study team members at the University of Gondar will be the primary data collectors with access to identifiable information and will keep the data identifier code link. University of Washington staff, however, may have access to data that contains patient identifiers in order to assist with data abstraction and conduct quality control audits and analysis. Identifiers include mother and or infant demographic information including names, date of birth, contact information, and location.

We may share de-identified data with the following procedures:
Investigators requesting access to data must sign a data-sharing agreement that provides for a commitment to: (1) using the data only for research purposes and not to identify any individual participant; (2) securing the data using appropriate computer technology; (3) not sharing the data with third parties and (4) destroying or returning the data after analyses are completed. We reserve the right to limit data provided to outside investigators if we believe there is a possibility of deductive disclosure of subjects with unusual characteristics. Disclosure will be provided in the enrollment consent forms for all subjects that data may be shared with collaborating researchers at the University of Washington and other institutions and that if the research purpose is not described in the consent form that the IRB must approve the research and determine if additional consent is required.

Anticipated Risks:

Risks of participation include risk of psychological/social distress associated with discussing newborn health and survival. If information about newborn health and development were disclosed, there is some risk of stigma or loss of status in the community.

The primary risk to the subjects is the potential for loss of confidentiality. If the subject's information was known, this could affect the standing for the subject in the community. We believe the risk of such disclosures is very low, however, due to the protections we will implement to ensure security. All study information will remain in confidential, secure files accessible only to the investigators and authorized study staff. All questionnaires and other study-related material will be labeled with an identification number, not their name. Data will be kept on a secure, password-protected computer behind a firewall that is located in a locked office at the University of Gondar. All study staff will undergo training on protecting the confidentiality of study subjects.

Anticipated Direct Benefits to Participants:
Subjects may benefit directly from the counseling and support that they receive from the intervention. Those who enroll in the prospective follow-up may benefit from knowing the health and growth status of the newborn that will be reported to participating mothers. Mothers and/or newborns judged to be in need of medical assessment or attention will be referred to a health facility, which may result in improved health, development, and survival.

Work Plan

We will conduct a series of lengthy training sessions with study staff prior to initiating the study. Topics covered will include definition of research, ethical considerations, scientific integrity, the informed consent procedure and its importance, and study procedures. These sessions will be conducted by a native Amharic speaker from the University of Gondar well versed in research procedures.