BMJ Open

Digital Health Tool to Improve Community Health Agent Performance for Child Development: A Randomized Controlled Trial in Peru
The C.H.E.S.T Project: Child Health Education and Surveillance Tool

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-028361
Article Type:	Protocol
Date Submitted by the Author:	05-Dec-2018
Complete List of Authors:	Westgard, Christopher; Elementos, Department of Research Rivadeneyra, Natalia; Elementos, Department of Research Rivas-Nieto, Andrea; Elementos, Department of Research Mechael, Patricia; HealthEnabled
Keywords:	maternal and child health, Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, early childhood develoment, Nutrition < TROPICAL MEDICINE, Community child health < PAEDIATRICS, community health worker

Digital Health Tool to Improve Community Health Agent Performance for Child Development: A Randomized Controlled Trial in Peru

The C.H.E.S.T Project:
Child Health Education and Surveillance Tool

Christopher Westgard[1*], Natalia Rivadeneyra[1], Andrea Rivas[1], Patricia Mechael[2]

[1]Department of Research, Elementos, Lima, Peru
[2] HealthEnabled, Cape Town, South Africa

[*]Corresponding Author:
Jiron Domeyer 105, Barranco, Lima, Peru
cmwestgard@gmail.com
+51.927.980.400

Word Count: 5227

1. ABSTRACT

Introduction: Cultivating good child development creates long-term impact on the well-being of the individual and society. The Amazon of Peru has high levels of many risk factors that are associated with poor child development, including chronic malnutrition, anemia, and poor educational opportunities. The use of 'community health agents' (CHA) can improve child developmental outcomes through health promotion, referral to health services, and surveillance. Information and communication technology can potentially increase the performance and impact of CHAs. However, there is a knowledge gap in how ICTs can impact child development in diverse settings, and the degree to which the programs can provide sustainable quality health services at scale.

Methods and Analysis: The current study will evaluate the impact of a tablet-based application (*Child Health Education and Surveillance Tool – The CHEST*) that intends to improve the performance of CHAs during their home visits with children under 4. The *CHEST* will guide the CHAs through the steps they need to follow to execute an effective home visit and provide videos and images to help teach key health messages. The *CHEST* will organize their caseload and provide a mechanism to record and report child health indicators. The impact will be evaluated through a quasi-experimental cluster randomized controlled trial. The data will be analyzed with a difference-in-difference estimation with the indicators of early childhood development, anemia, chronic malnutrition, knowledge of healthy child-rearing practices, and utilization of local health services. The study will be implemented in the Amazon region of Peru. The results of the study will provide evidence on the potential of a digital health tool to improve child health and development indicators in the region. The process evaluation with qualitative assessments will also be conducted to identify barriers, strengths, and weaknesses of the program.

Ethics and Dissemination: The protocol and instruments were approved by the Institutional Ethics Committee of the National Hospital of Mother and Children "San Bartolome" on Nov. 8, 2018 (IRB Approval #15463-18). The Trial identifier and registry name are: ISRCTN43591826 Issue Date: November 29, 2018. Original Protocol.

Keywords: mhealth, ICT, impact evaluation, maternal and child health, early childhood development, community health workers, Peru, Amazon.

2. STRENGTHS AND LIMITATIONS

- The results of the study will provide evidence on the potential of a digital health tool to improve the performance of community health agents
- The study will lend evidence to the effectiveness of community health agents to improve child health and development indicators in the region.
- A process evaluation with qualitative assessments will be used to identify issues of implementation and inform the implementation plan for scalability.
- The CHEST App will provide a surveillance mechanism that will allow for continuous feedback on the use of the intervention tool and health status of the study group.
- The greatest limitation of the study is due to the difficulties inherent to evaluating early childhood development by caregiver reporting.

3. BACKGROUND

In low and middle-low income countries millions of children under the age of 5 never reach their cognitive, linguistic and socio-emotional potential (1,2). Chronic malnutrition, anemia and iodine deficiency delay the physical and cognitive development of children, reduce their level of energy, and weaken their immune system. Cognitive development can also be delayed by low levels of early childhood stimulation (1,3). In the Peruvian Amazon there is a high prevalence of various risk factors associated with developmental delay, especially in rural areas. A study conducted in 2017 showed that the prevalence of developmental delay in the Amazon of Peru was 26.7% (4). In the Amazonian

department of Loreto, the prevalence of childhood anemia is 49.9% and chronic malnutrition is 23.6% (2017) (5). Those indicators are worse in indigenous communities (6–9).

The well-being of children in communities can be greatly increased by improving families' understanding of healthy child-rearing practices. Health promotion strategies that establish an intercultural dialogue with families do a better job at promoting healthy practices (10,11). A program can train and support community members to conduct health promotion that can create behavior changes and improve child development outcomes. Community Health Agents (CHA) can play an essential role in reducing inequalities in health services by acting as a link between communities and the local health services (11–13). The CHA can establish a warm relationship with the caregiver, thus increasing the acceptance of health advice, improving the absorption of knowledge and getting caregivers involved in the identification and resolution of their own health problems (14–21). The positive impact of CHAs has been associated with a reduction in malnutrition, anemia, malaria, cases of diarrhea, improved early childhood development, and other health indicators (11,22,23). Therefore, understanding and improving the performance of CHA can greatly enhance the health and well-being of communities (14,24–29).

Several studies have shown that a mobile information and communication technology (ICT) can improve the performance of CHAs in their ability to perform health promotion, collect and report timely information regarding family health, provide health services such as vaccines, and refer families to appropriate local health services (30–36). Additionally, when an ICT tool is used by a CHA, the device can increase the confidence the caregivers have in the messages being transmitted and increase the confidence the CHAs have in their own work (30,31,35–38). Through implementation science, innovations in ICT and maternal and child health can be adapted and leveraged to enable local contexts and spread the benefit of advancements in technology (33,34).

A study on the performance of CHA in the Peruvian Amazon identified difficulties they face in their work. They had difficulty providing a clear explanation of the causes of common diseases, remembering essential steps of home visits, and diversifying the health topics that were discussed (29). Studies have shown that a digital health tool could help CHA overcome the difficulties that arise during a home visit. However, there is currently a knowledge gap on the impact that such an intervention can have in diverse contexts, and how this type of technology can be best applied to improve health promotion by CHAs (27,39–42). Therefore, the present study aims to demonstrate the impact of a digital tool on CHA performance in the Peruvian Amazon and document the implementation process for replicability.

4. HYPOTHESIS

The study hypothesizes that a digital tool developed for the local context will improve the capacity of the CHA to transmit health messages to the caretakers, thus creating behavior change that will lead to better health and cognitive development for the children. The hypothesis is based on a theory of change that considers the potential outputs and outcomes that can be influenced by the intervention (43). The theory of change is displayed in Figure 1.

Figure 1. Theory of Change

Based on the Theory of Change, the study has the following hypotheses:

H1: The digital health device will improve the performance of CHAs during their home visits with children, as measured by doses, content, and inter-personal relationships.

H2: Improved performance by CHAs will increase knowledge acquisition and healthy child-rearing practices by care-givers.

H3: Improved knowledge and healthy practices by caregivers will improve the health and development of the child that receive the intervention.

5. OBJETIVOS

5.1. General Objective

The objective of the study is to evaluate the impact of the digital health tool (tablet with application) on cognitive development and nutrition status of children aged 10 to 48 months compared to children who receive home visits from CHA without the digital tool.

5.2. Specific Objectives

1. *[Primary Objective]* Improve child development scores in communication and gross motor in children by 20% compared to the baseline measurement.
    a. Children in the intervention group will experience a greater increase in child development scores in communication and gross motor than children in the control group ($p < 0.05$).
2. Decrease the prevalence of anemia in children by 20% compared to the baseline measurement.
    a. to. Children in the intervention group will experience a greater reduction in the prevalence of anemia than children in the control group ($p < 0.05$)
3. Decrease the prevalence of chronic malnutrition in children by 15%, compared to the baseline measurement.
    a. Children in the intervention group will experience a greater reduction in the prevalence of chronic malnutrition than children in the control group ($p < 0.05$).

The intermediate outcomes of the intervention include indicators of behavior change by CHA and families that have established causal connections with improved health and child development. The intervention is expected to achieve the following intermediate results:

4. The caregivers of the intervention group will improve knowledge evaluation scores by 50% compared to the baseline measurement.
    a. Caregivers in the intervention group will score higher on the knowledge evaluation than caregivers in the control group ($p < 0.05$).
5. CHAs in the intervention group will improve their performance evaluation scores by 50% compared to the baseline measurement.
    a. The CHAs in the intervention group will score higher on the performance evaluation than the CHAs in the control group. ($p < 0.05$).
6. The CHAs in the intervention group will score higher on a self-efficacy scale by 25% when compared to the baseline measurement.
    a. The CHAs in the intervention group will score higher on a self-efficacy scale than the CHAs in the control group ($p < 0.05$).
7. CHAs in the intervention group will increase the number of home visits per year by 25% compared to the baseline data.
8. The caregivers of the intervention group will use the local health services for children's health more frequently than the caregivers in the control group ($p < 0.05$).

6. METHODS

6.1. Study Design

The impact will be evaluated through a quasi-experimental cluster randomized controlled trial. Each cluster represents a community and will be matched with a second cluster by propensity score matching to create 1-1 pair matching. The propensity score will be determined by the size of the community, type of health facility in the community, and distance to the department capitol. For each cluster pair, one community will be randomly assigned to the intervention group and the other to the control group. The randomization will be conducted through computer-generated random numbers.

6.2. Location

The study will be implemented in the Amazon region of Peru. The study will be carried out in the department of Loreto, province of Maynas, and districts of Mazan and Punchana. The district of Mazan has a population of 13,779 (44), a prevalence of chronic malnutrition of 24.4% and a prevalence of anemia at 39.1%, in 2017 (45). The capital of the district of Mazan is located approximately one and a half hours by boat from the capitol city of the province, Iquitos. The district of Punchana has a population of 91,128 (44), a prevalence of chronic malnutrition of 22.7% and a prevalence of anemia of 39.9% (45). The capital of Punchana, is 20 minutes from the city of Iquitos.

The research team with the support of the Regional Ministry of Health of Loreto, will choose the communities that will be included in the study after traveling to the communities to ensure they meet the selection criteria. The study communities must have the following characteristics:

- Has an active CHA that visits families in their community.
- Is not a participant in another health related study.
- Is located less than 6 hours from Iquitos.
- Has at least 25 families and a maximum of 800 families.

6.3. Participants and Sample Size

The study population includes:

- 12 communities, 6 communities in the intervention group and 6 communities in the control group.
- 24 CHAs, approximately, half CHAs in the intervention group and half CHAs in the control group
- 200-400 children, approximately, half in the intervention group and one half in the control group

All children between 0 - 36 months in the communities will receive visits from a CHA, in the intervention and control group. However, only the CHAs in the intervention group will receive a tablet with the application to assist their home visits. All the children in the intervention group will have the opportunity to receive the intervention with the tablet.

To assess the impact of the intervention, a sample of the population will be chosen at random to receive the evaluation. The inclusion criteria for the study sample are the following:

- Children who belong to one of the communities included in the study, aged 6 to 36 months.
- Primary caregiver of the child is older than 16 years.

- The caregiver is willing to receive visits from the CHA.

The minimum age of children to be included in the impact evaluation is determined by the quality of the early childhood development tools. Assessement of early childhood development is more accurate with children older than 5 months (46). The maximum age of the children for the study is determined by the CHS program, which limits home visits by CHA to children up to 36 months old. The exclusion criteria for the study sample are:

- Families where the main caregiver or the child does not speak Spanish.
- Families that do not want to receive home visits from CHAs.
- Children with mental or physical disabilities.

Families that do not speak Spanish cannot be included because the study does not have appropriate translators for indigenous languages. Children with disabilities will be excluded in the evaluation because the cognitive development evaluation tool is not equipped to evaluate children with these conditions. However, children with disabilities will still receive the intervention.

The sample size for the evaluation (of children and caregivers) was calculated to identify the effect size on the primary outcome indicator, early childhood development. A study in the Amazon region of Peru (2017) collected data to determine that the proportion of children that are at-risk for developmental delay in communication or gross motor is 53.6% (data available in public repository) (4). To calculate the minimal sample size needed, the following parameters were determined:

- Two-sided significance level: 0.05
- Power: 80%
- Proportion at-risk of developmental delay in control group: 53.6%
- Ratio of sample size, intervention/control group: 1:1
- Proportion at-risk of developmental delay in intervention group (predicted): 42.4%

The total sample size is 698 children under the age of 4; 349 in intervention group and 349 in control group (Kelsey) (47). The study will add clusters until the desired sample size is reached. All participants in each cluster will be included in the baseline and follow-up survey.

6.4. **Instruments**

To measure the impact of the intervention and understand the perspective of the users, a series of instruments will be applied to the study participants. The instruments are early childhood development, attitudes and practices questionnaire, knowledge evaluation, performance evaluation of ACS, and collection of anemia and anthropometric indicators. Qualitative surveys will also be used to evaluate the satisfaction of CHAs and caregivers in relation to the intervention.

The surveys and evaluations will be carried out in the homes of the participants. The researcher will ask if a caregiver of a child within the age range is in the home, if so they will explain the study and ask the caregiver if they want to participant and are willing to sign the informed consent. The researcher will record the responses of the surveys and evaluation on a smart phone or electronic tablet.

6.4.1. Evaluation of Early Childhood Development

Early childhood development can be effectively evaluated with an instrument that utilizes caregiver-reported data to assess the ability of the child to perform age-relevant developmental activities (46,48–51). The current study will use the Caregiver-Reported Early Development Instrument (CREDI) to evaluate early childhood development (52,53). The CREDI has been validated as an effective instrument to evaluate early childhood development and identify developmental

delay, including low-resource settings in 17 countries (53). The CREDI is effective for large-scale, population-wide studies because it requires less time, materials, and evaluator expertise than other similar instruments (52).

The CREDI is conducted by asking the caregiver if the child is currently capable of completing a list of age-appropriate activities, in which the caregiver can respond by indicating; yes, no, or I don't know. The CREDI will provide a developmental score and a classification that represents the child's development trajectory as; normal development or at risk of developmental delay. These classifications will be used as the primary dependent variables of the study.

6.4.2. Attitudes and Practices Questionnaire

The study will use a quantitative questionnaire to measure the attitudes and practices of caregivers that influence maternal and child health. The following topics are included in the questionnaire: demographic information, safe pregnancy practices, dietary practices, prevention of illnesses, early childhood stimulation, and use of local health services. The questionnaire will be conducted with all caregivers of the children included in the study. The questionnaire will take approximately 10 minutes.

6.4.3. Knowledge Evaluation

To assess the knowledge of caregivers of healthy practices for maternal and child health, an instrument was built based on the literature (13,54–56). The Knowledge Evaluation asks the caregiver questions regarding maternal and child health, nutrition, sanitation, and infectious diseases. The questions are open-ended to give the caregiver the opportunity to provide multiple answers that displays their knowledge of the topic.

The Knowledge Evaluation will take place directly after the Attitudes and Practices Questionnaire. The Knowledge Evaluation will be scored by giving the participant 1 point for every correct answer they provide. The correct answers will be added together to provide a total "Knowledge Score" for the caregiver.

6.4.4. Performance Evaluation of CHAs

The Performance Evaluation of CHAs was based on an instrument built by the University of West Indies and the Inter-American Development Bank to measure the quality of home visits by CHAs (14). The Performance Evaluation includes questions related to the use of materials, activities, promotion of early childhood development, relationship between CHA and caregivers, and relationships between the CHA and the child. The Performance Evaluation was modified and validated during a previous study in the Amazon region within the local CHA program. The instrument provides further focus on health messages provided by the CHA and the needs of the communities in the Amazon (29).

The conduct the performance evaluation, the researcher will accompany the CHA on their home visit with a child to observe the home visit. The researcher will observe the home visit in silence, trying not to influence the dynamic of the visit. The researcher will take notes during the visit and complete the Performance Evaluation immediately after the conclusion of the home visit.

6.4.5. Survey of the Use of Local Health Services

The research team will survey the local health centers in the communities to obtain statistics regarding the use of health services related to maternal and child health, including: child growth monitoring check-ups, prenatal check-ups, immunization coverage, distribution of micronutrient supplements, distribution of anti-parasitic medicine, and distribution of oral rehydration salts for

diarrhea. The survey will be conducted with the nurse that conducts maternal and child health evaluations at the health center. The survey will take approximately 15 minutes and can be filled out independently by the health post representative.

6.4.6. Survey of Child Health Indicators

The CHEST application will be used to collect child health indicators by CHAs during their home visits. The children have a card with information that was recorded during their growth monitoring check-ups at the local health center, including height, weight, age, vaccines, and hemoglobin levels (when tested). The CHA will observe the information written on the card and record it with the CHEST application. The CHA will also ask additional questions regarding the health of the child, including incidences of diarrhea, cough, fever, malaria and other illness. The data from the application will be uploaded to the secured server when the CHA or supervisor has access to the cellular network.

6.4.7. Questionnaire on Satisfaction and Self-Efficacy of CHA

The Questionnaire on Satisfaction and Self-Efficacy of CHA will be used to measure the degree satisfaction and self-efficacy the CHAs have from using the CHEST application during their home visits. The questions are both quantitative and qualitative. The CHAs will have the opportunity to describe how the experience with the tablet could be improved.

6.4.8. Questionnaire on Satisfaction of Caregiver

The Questionnaire on Satisfaction of caregivers will be used to measure the degree satisfaction of the caregivers that received the intervention. The questions are both quantitative and qualitative. The caregivers will have the opportunity to describe what they like and don't like about the use of a tablet during the home visits.

6.5. **Patient and Public Involvement**

The study was created through formative research done in the same communities to identify their needs and desires related to improving child health and development. A performance evaluation study was conducted with the CHAs in the region by the author (29). In the study, the CHAs and caregivers expressed their need and desire for more information regarding topics of health and child development. The current intervention was created to address those needs.

The results of the study will be presented to the participants, including the community health agents, caregivers, health facility personal, and Regional Ministry of Health in the form of a study brief that indicates the results of each indicator collected. The results will be presented to the public via publication of results in an international scientific journal.

Patients were not involved in the design or recruitment of the study.

7. INTERVENTION

The intervention includes the development and implementation of a tablet-based application (CHEST) to improve the performance of the CHAs during their home visits. The CHAs will use the CHEST Application during their home visits to teach caregivers good health practices and early childhood stimulation. The application will provide the steps for the CHA to follow to conduct an effective home visit. The application will include videos and images to show the caregiver to transmit key health messages. Also, the application will organize the case load of children of the CHA and will provide a mechanism to record maternal and child health indicators.

The intervention is described in the following five phases:

7.1. **Phase 1: Preparation of Material**

7.1.1. Step-by-Step Agendas for Home Visits

The research team will work with the Regional Ministry of Health of Loreto to build agendas for home visits by the CHAs. The health messages for the home visits are based on national and international manuals for home visits by CHAs to teach maternal and child health and development (57–60). The agendas include steps to follow by the CHA to provide a quality home visit and collect child health indicators. The messages included in the agendas include; what nutritious foods should be consumed by children, how to avoid diarrhea and other diseases, good practices of early attention, and use of health services. There will be 1 agenda for each month of age of the child (1-36 months).

7.1.2. Multimedia Material

The research team will generate multimedia material to be used in the application to transmit health messages. The content will be designed to convey the health messages clearly within the local culture in the Amazon. The material will include videos of people from the region acting out health topics, instructional videos on early childhood stimulation, and animations that describes health issues. In addition, the application will include educational images that have been developed by the regional Ministry of Health of Loreto and other institutions.

7.2. **Phase 2: Development of the Application**

The research team will evaluate the mhealth applications that have been developed and are open source to determine which will be best to adapt for the current project. The project will contract a team of program developers to modify the open source application to fit the current objectives and local context. The program developer will include the agendas, multimedia, and data collection mechanisms in the application. The application will function without internet signal and protect all information by password.

7.3. **Phase 3: Baseline Data Collection**

The research team will conduct the surveys and evaluations in the intervention and control communities to obtain a baseline for the study. The instruments that will be applied for the baseline survey include the *Early Childhood Development Evaluation, Attitudes and Practices Questionnaire, Knowledge Evaluation, Performance Evaluation of CHA, and Survey on the Use of Health Services*. The baseline survey will be completed before implementation beings in the intervention and control communities.

7.4. **Phase 4: Implementation of Intervention**

7.4.1. Training Workshops

The research team will conduct training workshops with the CHAs in the intervention group to teach them how to use the tablet and application. The workshops will occur during a period of 3 days, 4 hours per day. The leaders of the health facility and Regional Ministry of Health of Loreto will be invited to participate in the workshops and in the supervision of the development of the project.

7.4.2. Distribution of Tablets

After the training workshops, the research team will give a tablet to each CHA in the intervention communities. The CHAs will continue with their normal activities of conducting home visits with the children in their caseload. The number of home visits will depend on the program that currently exists in the community. The only change is that the CHAs will use the tablets during the home

visits. The CHAs will be instructed to bring the tablet to local health center if they are having problems with the tablet or to store the tablet in their home until a member of the monitoring team visits their community.

7.4.3. Monitoring

The research team will supervise the work of the CHAs through observations of their home visits and interviews with families and CHAs in the communities. The research team will visit the communities every month during the first 4 months, and less frequently when they see that the program is working as it should.

The team will also track activities of the CHAs through the data uploaded by the application. They will be able to track the number of visits being conducted and the health indicators of the children. If the tablet is not uploading data to the survey, the research team will visit the community to identify the problem.

The local health facility will also have access to the data and will be able to identify if a child is at risk of chronic malnutrition, chronic diarrhea and/or is not attending growth monitoring check-ups.

7.5. **Phase 5: Evaluation of the Intervention**

At the end of the intervention, the follow-up survey will be carried out in the intervention and control communities. The instruments included in the follow-up survey include the *Evaluation of Early Childhood Development, Attitudes and Practices Questionnaire, Knowledge Test, Performance Evaluation of CHA, Survey of Use of Health Services, Questionnaire on Satisfaction and Self-Efficacy of CHA*, and *Questionnaire on Satisfaction of Caregivers*.

The data gathered by the application will be used to evaluate the child heath indicators and the number of home visits conducted.

8. DATA ANALYSIS

The quantitative data obtained in the surveys will be organized and analyzed with the statistical software, Epi Info version 7.1.4.0 (61). The qualitative data will be organized and analyzed with the program Atlas.ti (62). To carry out the impact analysis, four mathematical models will be used to interpret the results, generating an optimal analysis to understand the interactions between the variables. First, a descriptive analysis will be performed to compare indicators between the analysis groups, including average and frequencies of the independent and dependent variables. Second, a bivariate analysis with Chi-square test will be done to examine the associations between the independent and the dependent variables. Third, a multivariate regression analysis will be used to examine the interactions between the independent variables and the dependent variables. Fourth, a difference-in-difference analysis will be used to calculate the impact of the intervention.

Impact = (Follow-up survey results in the intervention group – baseline survey results in intervention group) - (Follow-up survey results in control group – baseline survey results in control group)

The difference-in-difference estimation will be conducted with each of the objective indicators: early childhood development scores, prevalence of anemia, and prevalence of chronic malnutrition.

8.1. **Data Monitoring**

Data monitoring will be completed by the Data Monitoring Committee to ensure non-biased handling and analysis of data obtained from baseline, monitoring, and follow-survey. The Data Monitoring Committee will be made up of the team of experts that will be hired to create the

content of the intervention and mentors that guided the research team. The Data Monitoring Committee will each guard files of data at different time points so they can later be crossed reference to ensure consistency. The Data Monitoring Committee will not include permanent members of the sponsor organization or associates of the funding organization or anyone with competing interest or incentive for the intervention to be successful.

The datasets generated during and/or analysed during the current study will be stored in the publically available repository, figshare (https://figshare.com/). De-identified participant data, including early childhood development evaluation scores, anemia results, chronic malnutrition results, KAP survey results, and CHA performance evaluations, will be stored in the repository. The data will be available through the repository for 10 years. Data from participants will only be made available if consent was provided by the participant through the informed consent process.

9. ETHICAL CONSIDERATIONS

The investigation was approved by the Ethics Committee of the National Hospital "San Bartolomé" on November 8, 2018 (Exp. Number 15463-18, Oficio N. 0744-2018-OADI-HONADOMANI-SB)

The investigation will include only those individuals that are willing and able to give their consent to be included in the study. The participant must be able to understand the information presented to them and voluntarily express their choice of whether they want to participate or not. The caregivers must be over 15 years of age to participate in the study.

It will be clearly stated that participation in the study will not compromise the health of the participants or violate any rights of the child. There will be no financial compensation for participation in the study. No biological samples will be collected, nor any medical or pharmacological treatments delivered in the research process. There are no possible adverse effects associated with participation in the study. There is the possibility of generating discomfort in the participants because the visits and surveys imply an investment of time. Given this, participants will be informed about the amount of time involved for their participation in the survey before signing the informed consent.

After completion of the child development evaluation the results will be immediately shared with the caretaker along with recommendations of early childhood stimulation activities that could benefit the child. Likewise, the results of the evaluations will be communicated to the health center of the community with a copy of a list of the children who are at risk of developmental delay. The child development evaluation represents a direct benefit to the participants in the intervention and control group.

The results obtained from the study will be made publicly accessible through the publication of finding and a report delivered to the local health authorities. The dataset will available in a public data repository.

9.1. **Informed consent for caregivers**

The Informed Consent for Caregivers includes the description of the study, the participation of the caregiver, the participation of the child, and the amount of time required to complete the survey. The interviewer that conducts the questionnaires will ask for consent from the caregiver. If the caregiver agrees to participate in the study, they will be asked to sign the Informed Consent form. The caregiver will be provided a copy of the consent.

9.2. Informed consent for CHA

The Informed Consent for CHAs includes a description of the study and the performance evaluation that will be conducted with the CHA. The interviewer that conducts the questionnaires will ask for consent from the CHA. If the CHA agrees to participate in the study, they will be asked to sign the Informed Consent for CHA. The CHA will be offered a copy of the consent.

9.3. Data security

All data will be stored in a secure encrypted server that is protected by password. All identifiable information in the data set will be deleted to make it impossible to link the data with the individual. Information regarding contact information of CHAs will be stored on the secure server. There will be no need to maintain identifies within the data because there will be no follow-up serves with individuals. Members of the Data Monitoring Committee will ensure all identifiable information has been removed from the data set.

9.4. Competing interests

The authors and members of the research team have no competing interest.

10.CHRONOLOGY

The study will last 24 months, beginning in October 2018 and ending in September 2020. The schedule of activities can be found in Table 1.

Table 1: Schedule of Activities

Activity	Oct	Nov	Dec	Jan '19	Feb	Mar	Apr	May	June-Sept	Oct-Jan '20	Feb-Apr	May-July	Aug, '20
Complete Ethics Committee Protocol													
Develop home visit agendas													
Validate home visit material													
Create videos													
Develop Application													
Validate Application													
Recruit participants													
Baseline Survey													
Train CHAs													
Deploy App													
Monitoring													
Final Evaluation													
End of Project													

10.1. Flow Diagram schedule of activities

The Flow Diagram in Table 2 describes when intervention allocation and assessments of the study population will take place, in relation to the study activities.

Table 2: Flow Diagram

	Study Period				
	Enrolment	**Allocation**	***Post-Allocation***		***Close-out***
TIMEPOINT	$-t_1$	**0**	t_1	t_2	t_x
ENROLMENT:					

Eligibility screen of inclusion and exclusion criteria	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
Distribution of Tablet			←	—	→
Control group			←	—	→
ASSESSMENTS:					
Early childhood development evaluation	X				X
Performance Evaluation	X				X
Knowledge, Attitudes, and Practices Survey	X				X
Monitoring of Community Health Agents		X	X	X	

11.FUNDING

The study is funded by the grant, Saving Brains, by Grand Challenges, Canada (63). The funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

12. AUTHOR CONTRIBUTIONS

CW conceived of the study. CW, NR, AR, and PM contributed to the writing and revision of the protocol. PM provided advisory on study design. All authors contributed to refinement of the study protocol and approved the final manuscript.

13. TRAIL SPONSOR

Trail Sponsor: Elementos
Contact Name: Christopher Westgard
Address: Jiron Domeyer, Barranco, Lima, Peru
Telephone: +51927980400
Email: cmwestgard@gmail.com

14.BIBLIOGRAPHY

1. Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B. Developmental potential in the first 5 years for children in developing countries. The Lancet. 2007 Jan 6;369(9555):60–70.

2. Engle PL, Black MM, Behrman JR, Mello MC de, Gertler PJ, Kapiriri L, et al. Strategies to avoid the loss of developmental potential in more than 200 million children in the developing world. The Lancet. 2007 Jan 20;369(9557):229–42.

3. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. Lancet Lond Engl. 2011 Oct 8;378(9799):1325–38.

4. Westgard C, Alnasser Y. Developmental delay in the Amazon: The social determinants and prevalence among rural communities in Peru. PloS One. 2017;12(10):e0186263.

5. Instituto Nacional de Estadistica e Informatica. Loreto Compendio Estadistico 2017. Sistema Estadistico Nacional; 2017.

6. Anticona C, San Sebastian M. Anemia and malnutrition in indigenous children and adolescents of the Peruvian Amazon in a context of lead exposure: a cross-sectional study. Glob Health Action. 2014;7:22888.

7. Díaz A, Arana A, Vargas-Machuca R, Antiporta D. Situación de salud y nutrición de niños indígenas y niños no indígenas de la Amazonia peruana. US11 [Internet]. 2015 [cited 2017 Jan 26]; Available from: http://iris.paho.org/xmlui/handle/123456789/10008

8. Flores-Bendezu J, Calderon J, Rojas B, Alarcon-Matutti E, Gutierrez C. Chronic malnutrition and anemia in children under 5 years of indigenous households of Peru - Analysis of Demographic and Health Survey 2013. Fac Med 2015762135-40 Dxdoiorg1015381analesv76i211139.

9. Grantham-McGregor SM, Fernald LCH, Kagawa RMC, Walker S. Effects of integrated child development and nutrition interventions on child development and nutritional status. Ann N Y Acad Sci. 2014 Jan;1308:11–32.

10. Perry HB, Sacks E, Schleiff M, Kumapley R, Gupta S, Rassekh BM, et al. Comprehensive review of the evidence regarding the effectiveness of community–based primary health care in improving maternal, neonatal and child health: 6. strategies used by effective projects. J Glob Health [Internet]. [cited 2017 Nov 9];7(1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5491945/

11. Gilmore B, McAuliffe E. Effectiveness of community health workers delivering preventive interventions for maternal and child health in low- and middle-income countries: a systematic review. BMC Public Health. 2013 Sep 13;13:847.

12. Global Health Workforce Alliance, World Health Organization. Global experience of community health workers for delivery of health related millennium development goals: a systematic review, country case studies, and recommendations for integration into national health systems. 2010.

13. The Earth Institute. Millennium Villages Project. Community Health Worker Trainer's Manual. A guide to Home Based Services [Internet]. Version 2.1. Columbia University; 2013. Available from: http://millenniumvillages.org/wp-content/uploads/2014/09/CHWTrainingManual.pdf

14. Leer J, Lopez-Boo F, Perez Exposito A, Powell C. A Snapshot on the Quality of Seven Home Visit Parenting Programs in Latin America and the Caribbean. Inter-American Development Bank; 2016.

15. Schodt S, Parr J, Maria CA, Rubio-Codina M. La medición de la calidad de os servicios de visitas domiciliarias . Una revisión de la literatura. Danco Interamericano de Desarrollo; 2015.

16. Vogel CA, Caronongan P, Thomas J, Bandel E, Xue Y, Henke J, et al. Toddlers in Early Head Start: A Portrait of 2-Year-Olds, Their Families, and the Programs Serving Them. Volume 1: Age 2 Report. OPRE Report 2015-10 [Internet]. Administration for Children & Families; 2015 [cited 2017 Aug 3]. Available from: https://eric.ed.gov/?id=ED558558

17. Roggman LA, Cook GA, Innocenti MS, Jump Norman V, Boyce LK, Christiansen K, et al. Home Visit Quality Variations in Two Early Head Start Programs in Relation to Parenting and Child Vocabulary Outcomes. Infant Ment Health J. 2016 May 1;37(3):193–207.

18. Medina A, Sofía I. Evaluation protocol application of tasks for the socio - cognitive development in children from 37 to 71 months in the Program of Comprehensive Attention to Early Childhood Modality Family Environment District Secretariat of Social Integration [Internet]. [cited 2017 Aug 3]. Available from: https://intellectum.unisabana.edu.co/handle/10818/23587

19. Fernández S, Yonah R. Aplicación de ensayos domiciliarios para evaluar la adopción de prácticas mejoradas de alimentación complementaria en madres. Centro materno infantil Juan Pablo II. Villa El Salvador, Lima. 2005. Univ Nac Mayor San Marcos [Internet]. 2007 [cited 2017 Aug 4]; Available from: http://cybertesis.unmsm.edu.pe/handle/cybertesis/1121

20. Walker SP, Powell C, Chang SM, Baker-Henningham H, Grantham-McGregor S, Vera-Hernandez M, et al. Estrategias de apoyo parental a través de los servicios de salud en el Caribe [Internet]. BID; 2016 Feb [cited 2017 Aug 3]. Available from: http://repositorio.minedu.gob.pe/handle/123456789/4112

21. Chang-Say Chong A. La comunicación en los proyectos de lucha contra la desnutrición crónica infantil : el caso Ally Micuy (Áncash). Pontif Univ Católica Perú [Internet]. 2014 Sep 25 [cited 2017 Aug 3]; Available from: http://tesis.pucp.edu.pe/repositorio/handle/123456789/5598

22. Lewin S, Munabi-Babigumira S, Glenton C, Daniels K, Bosch-Capblanch X, Wyk BE van, et al. Lay health workers in primary and community health care for maternal and child health and the management of infectious diseases. Cochrane Database Syst Rev [Internet]. 2010 [cited 2018 Sep 20];(3). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004015.pub3/abstract

23. Lassi ZS, Kumar R, Bhutta ZA. Community-Based Care to Improve Maternal, Newborn, and Child Health. In: Black RE, Laxminarayan R, Temmerman M, Walker N, editors. Reproductive, Maternal, Newborn, and Child Health: Disease Control Priorities, Third Edition (Volume 2) [Internet]. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2016 [cited 2016 Jun 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK361898/

24. Howard KS, Brooks-Gunn J. The role of home-visiting programs in preventing child abuse and neglect. Future Child. 2009;19(2):119–46.

25. Singh V, Ahmed S, Dreyfuss ML, Kiran U, Chaudhery DN, Srivastava VK, et al. Non-governmental organization facilitation of a community-based nutrition and health program: Effect on program exposure and associated infant feeding practices in rural India. PloS One. 2017;12(9):e0183316.

26. Swider SM. Outcome Effectiveness of Community Health Workers: An Integrative Literature Review. Public Health Nurs. 2002 Jan 1;19(1):11–20.

27. Agarwal S, Perry HB, Long L-A, Labrique AB. Evidence on feasibility and effective use of mHealth strategies by frontline health workers in developing countries: systematic review. Trop Med Int Health TM IH. 2015 Aug;20(8):1003–14.

28. Mobile Healthcare Information for All. Assessment of mHealth applicaitons for their potential to provide essential healthcare information for citizens in low resource settings. HIFA; 2017.

29. Westgard C, Naraine R, Paucar Villacorta DM. Performance Evaluation of Community Health Workers: Case Study in the Amazon of Peru. J Community Health. 2018 Mar 26;

30. Ilozumba O, Dieleman M, Kraamwinkel N, Belle SV, Chaudoury M, Broerse JEW. "I am not telling. The mobile is telling": Factors influencing the outcomes of a community health worker mHealth intervention in India. PLOS ONE. 2018 Mar 27;13(3):e0194927.

31. van Heerden A, Sen D, Desmond C, Louw J, Richter L. App-Supported Promotion of Child Growth and Development by Community Health Workers in Kenya: Feasibility and Acceptability Study. JMIR MHealth UHealth [Internet]. 2017 Dec 5 [cited 2018 Sep 19];5(12). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5736876/

32. Lee S, Chib A, Kim J-N. Midwives' Cell Phone Use and Health Knowledge in Rural Communities. J Health Commun. 2011 Oct 1;16(9):1006–23.

33. Peterson HB, Haidar J, Fixsen D, Ramaswamy R, Weiner BJ, Leatherman S. Implementing Innovations in Global Women's, Children's, and Adolescents' Health: Realizing the Potential for Implementation Science. Obstet Gynecol. 2018 Mar;131(3):423–30.

34. Peterson HB, Haidar J, Merialdi M, Say L, Gülmezoglu AM, Fajans PJ, et al. Preventing maternal and newborn deaths globally: using innovation and science to address challenges in implementing life-saving interventions. Obstet Gynecol. 2012 Sep;120(3):636–42.

35. Källander K, Tibenderana JK, Akpogheneta OJ, Strachan DL, Hill Z, Asbroek AHA ten, et al. Mobile Health (mHealth) Approaches and Lessons for Increased Performance and Retention of Community Health Workers in Low- and Middle-Income Countries: A Review. J Med Internet Res. 2013;15(1):e17.

36. Prinja S, Nimesh R, Gupta A, Bahuguna P, Gupta M, Thakur JS. Impact of m-health application used by community health volunteers on improving utilisation of maternal, new-born and child health care services in a rural area of Uttar Pradesh, India. Trop Med Int Health TM IH. 2017;22(7):895–907.

37. Chib A. The Aceh Besar midwives with mobile phones project: Design and evaluation perspectives using the information and communication technologies for healthcare development model. J Comput-Mediat Commun. 2010 Apr 1;15(3):500–25.

38. Limaye NP, Rivas-Nieto AC, Carcamo CP, Blas MM. Nuestras Historias- Designing a novel digital story intervention through participatory methods to improve maternal and child health in the Peruvian Amazon. PLOS ONE. 2018 Nov 5;13(11):e0205673.

39. Agarwal S, Rosenblum L, Goldshmidt T, Carras M, Goal N, Labrique AB. Mobile Technology in Support of Frontline Health Workers. Johns Hopkins University Global mHealth Initiative; 2016.

40. Batavia H, Kaonga N. mHealth Support Tools for Improving the Performance of Frontline Health Workers. An Invesntory and Analytical Review. mHealth Alliance; 2014.

41. Piette JD, Lun KC, Moura LA, Fraser HSF, Mechael PN, Powell J, et al. Impacts of e-health on the outcomes of care in low- and middle-income countries: where do we go from here? Bull World Health Organ. 2012 May 1;90(5):365–72.

42. Mookherji S, Mehl G, Kaonga N, Mechael P. Unmet Need: Improving mHealth Evaluation Rigor to Build the Evidence Base. J Health Commun. 2015;20(10):1224–9.

43. Lafferty CK, Mahoney CA. A Framework for Evaluating Comprehensive Community Initiatives. Health Promot Pract. 2003 Jan 1;4(1):31–44.

44. Instituto Nacional de Estadistica E Informatica. Estadisticas. Poblacion y Vivienda. Poblacion Ttoal al 30 de Junio, POr Grupos Quinquenales de Edad, Segun Departamento, Provincia y Distrito, 2015 [Internet]. 2015. Available from: https://www.inei.gob.pe/estadisticas/indice-tematico/poblacion-y-vivienda/

45. Instituto Naciona De Salud. Sistema de informacion del estado nutricional (SIEN). 2017 [Internet]. Available from: https://web.ins.gob.pe/es/alimentacion-y-nutricion/vigilancia-alimentaria-y-nutricional/vigilancia-del-sistema-de-informacion-del-estado-nutricional-en-%20EESS

46. Rubio-Codina M, Araujo MC, Attanasio O, Muñoz P, Grantham-McGregor S. Concurrent Validity and Feasibility of Short Tests Currently Used to Measure Early Childhood Development in Large Scale Studies. PLOS ONE. 2016 Aug 22;11(8):e0160962.

47. Kelsey J, Whittemore A, Evans A, Thompson D. Methods in Observational Epidemiology. Monographs in Epidemiology and Biostatistics. Second Edition. Vol. 26. New York: Oxford University Press; 1996.

48. Fernald LCH, Kariger P, Hidrobo M, Gertler PJ. Socioeconomic gradients in child development in very young children: evidence from India, Indonesia, Peru, and Senegal. Proc Natl Acad Sci U S A. 2012 Oct 16;109 Suppl 2:17273–80.

49. Fernald L, Kariger P, Engle P, Raikes A. Examining Early Child Development in Low-Income Countries: A Toolkit for the Assessment of Children in the First Five Years of Life. The World Bank; 2009.

50. Rubio-Codina M, Araujo MC, Attanasio O, Grantham-McGregor S. Validez concurrente y viabilidad de pruebas cortas comunmente usadas para medir el desarrollo infantil temprano en estudios a gran escala: Metodologia y resultados. Banco Interam Desarro [Internet]. 2016 Agosto;(723). Available from: https://publications.iadb.org/bitstream/handle/11319/7823/Validez-concurrente-y-viabilidad-de-pruebas-cortas-comunmente-usadas-para-medir-el-desarrollo-infantil-temprano-en-estudios-a-gran-escala-metodologia-y-resultados.pdf

51. Rubio-Codina M, Attanasio O, Grantham-McGregor S. Mediating pathways in the socio-economic gradient of child development: Evidence from children 6–42 months in Bogota. Int J Behav Dev. 2016 Nov 1;40(6):483–91.

52. McCoy DC, Waldman M, Fink G. Measuring early childhood development at a global scale: Evidence from the Caregiver-Reported Early Development Instruments. Early Child Res Q. 2018 Oct 1;45:58–68.

53. McCoy DC, Fink G, Pierre-Louis M. CREDI. Caregiver-Reported Early Development Instruments. User Guide. [Internet]. 2018. Available from: sites.sph.harvard.edu/credi/

54. Tran NT, Portela A, de Bernis L, Beek K. Developing Capacities of Community Health Workers in Sexual and Reproductive, Maternal, Newborn, Child, and Adolescent Health: A Mapping and Review of Training Resources. PLoS ONE [Internet]. 2014 Apr 15 [cited 2017 Jul 21];9(4). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3988080/

55. Crigler L, Hill K, Furth R, Bjerregaard D. Community Health Worker Assessment and Improvement Matrix (CHW AIM): A Toolkit for Improving Community Health Worker Programs and Services. Revised Version. Published by the USAID Health Care Improvement Project. Bethesda, MD: University Research Co., LLC (URC). 2013.

56. Basic Support for Institutionalizing Child Survival (BASICS) and the Prevention of Postpartum, Hemorrhage Initiative (POPPHI). Training Community Health Workers to Give Maternal and Newborn Health Messages: A Guide for Trainers. Arlington, Va., USA: for the United States Agency for International Development (USAID). 2009.

57. Perry H, Crigler L. Developing and Strengthening Community Health Worker Programs at Scale: a reference guide and case studies for program managers and policymakers. [Internet]. Maternal and Child Health Integrated Program; 2014. Available from: http://www.mchip.net/CHWReferenceGuide

58. Ministerio de Salud. Preparando al Agente COmunitario de Salud para el Cuidado Integral de la Salud y Nutricion de las Gestantes y de las Niñas y Niños Menores de 5 años - "El Manual del Agente Comunitario de Salud." Ministerio de Salud del Peru; 2009.

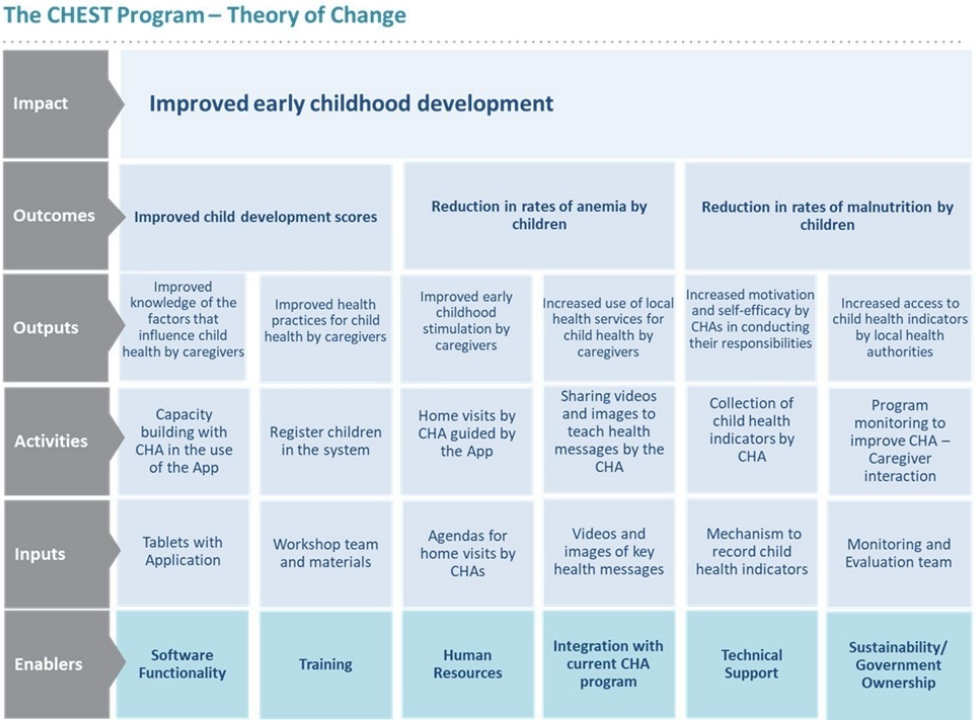
59. Ministerio de Salud DG de P de la S. Orientaciones Para El Fortalecimiento de la Labor Del Agente Comunitario de Salud. Ministerio de Salud del Peru; 2014.

60. Organizacion Panamerican de la Salud. Manual del Agente Comunitario de Salud: Manual del Facilitador. Organizacion Mundial de la Salud; 2010.

61. Epi Info™ | CDC [Internet]. 2017 [cited 2018 Sep 13]. Available from: https://www.cdc.gov/epiinfo/index.html

62. ATLAS.ti: The Qualitative Data Analysis & Research Software [Internet]. [cited 2018 Sep 13]. Available from: https://atlasti.com/

63. Saving Brains - Unlocking the Potential for Development [Internet]. Grand Challenges Canada. [cited 2018 Aug 25]. Available from: http://www.grandchallenges.ca/programs/saving-brains/



261x190mm (96 x 96 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	___2 and 11___
	2b	All items from the World Health Organization Trial Registration Data Set	__2 and 12____
Protocol version	3	Date and version identifier	__2_____
Funding	4	Sources and types of financial, material, and other support	__12_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	__12_____
	5b	Name and contact information for the trial sponsor	__12_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	__12_____
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	__12_____

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	__2-4_____
	6b	Explanation for choice of comparators	__10-11_____
Objectives	7	Specific objectives or hypotheses	___5_____
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	___5-7_____
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	__5-6_____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	___6_____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	___9-10_____
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	____NA_____
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	___10_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	___NA_____
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	____4-5_____
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	____12-13___

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	__6-7_____
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	___6_____
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	___5_____
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	__NS_____
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	___5_____
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	____NA_____
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	___NA_____
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	__7-11_____
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	____10-11_____

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	_____11___
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	____11_____
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	____NA_____
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	____NA_____
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	___11_____
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	___11_____
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	____NA_____
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	____NA_____
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	___11_____
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	___NA_____

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	___12_____
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	___NA_____
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	___12_____
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	___12_____
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	___12_____
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	___NA_____
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	___12_____
	31b	Authorship eligibility guidelines and any intended use of professional writers	___NA_____
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	___12_____
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	___NA_____
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	___NA_____

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

An mHealth Tool to Improve Community Health Agent Performance for Child Development: A Cluster-Randomized Controlled Trial in Peru

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-028361.R1
Article Type:	Protocol
Date Submitted by the Author:	06-May-2019
Complete List of Authors:	Westgard, Christopher; Elementos, Department of Research Rivadeneyra, Natalia; Elementos, Department of Research Mechael, Patricia; HealthEnabled
Primary Subject Heading:	Global health
Secondary Subject Heading:	Health services research, Research methods
Keywords:	maternal and child health, Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, early childhood develoment, Nutrition < TROPICAL MEDICINE, Community child health < PAEDIATRICS, community health worker

An mHealth Tool to Improve Community Health Agent Performance for Child Development: A Cluster-Randomized Controlled Trial in Peru

Christopher Westgard*
Elementos, Lima, Peru
cmwestgard@gmail.com

Natalia Rivadeneyra
Elementos, Lima, Peru
rivadeneyra.natalia@gmail.com

Patricia Mechael
HealthEnabled, Cape Town, South Africa
patty@healthenabled.org

*Corresponding Author:
Jiron Domeyer 105, Barranco, Lima, Peru
cmwestgard@gmail.com
+51.927.980.400

Word Count: 5227

1. ABSTRACT

Introduction: Cultivating good child development creates long-term impact on the well-being of the individual and society. The Amazon of Peru has high levels of many risk factors that are associated with poor child development. The use of 'community health agents' (CHAs) can potentially improve child development outcomes. Mobile information and communication technology (ICT) can potentially increase the performance and impact of CHAs. However, there is a knowledge gap in how mobile ICT can impact child development in low resource settings.
Methods and Analysis: The current study will evaluate the impact of a tablet-based application (App) that intends to improve the performance of CHAs during their home visits with children under 4. The App will guide the CHAs through the steps of an effective home visit and provide images and videos to help teach key health messages. The App will organize their caseload and provide a mechanism to record and report child health indicators. The impact will be evaluated through an experimental cluster randomized controlled trial. The clusters will be assigned to the intervention or control group based on a covariate-constrained randomization method. The impact on child development scores, anemia, and chronic malnutrition will be assessed with an analysis of covariance (ANCOVA). Secondary outcomes of knowledge of healthy child-rearing practices, self-efficacy, and use of health services will be compared between baseline and follow-up. The study will be implemented in the Amazon region of Peru. The results of the study will provide evidence on the potential of a mHealth tool to improve child health and development indicators in the region.
Ethics and Dissemination: The protocol and instruments were approved by the Institutional Ethics Committee of the National Hospital of Mother and Children "San Bartolome" on Nov. 8, 2018 (IRB Approval #15463-18). The trail is registered in the ISRCTN Registry at, ISRCTN43591826.

Keywords: mHealth, ICT, impact evaluation, maternal and child health, early childhood development, community health workers, Peru, Amazon, community health workers.

2. ARTICLE SUMMARY

2.1. Strengths and Limitations of This Study

- The intermediate variables that will be assessed in the study will provide data on each step in the theory of change. We will be able to evaluate each process that leads to the behavior change.
- A process evaluation with qualitative assessments will be used to identify issues of implementation and inform the implementation plan for scalability.
- The mHealth tool and the monitoring and evaluation strategy provides a surveillance mechanism that will allow for continuous feedback on the use of the intervention tool and health status of the study group.
- The baseline and survey strategy allow for the child development indicators, child health indicators, knowledge evaluations, and social determinants surveys to be collected during one visit, thus reducing the opportunity for error in data reporting, organizing, and analyzing.
  Child development will be assessed by a parent reported survey. Although the instrument has been shown to have high correlation to directly observed survey, there is more potential for parent created biased.

3. BACKGROUND

In low and middle-low income countries millions of children under the age of 5 never reach their cognitive, linguistic and socio-emotional potential (1,2). Chronic malnutrition, anemia and iodine deficiency delay the physical and cognitive development of children, reduce their level of energy, and weaken their immune system. Child development can also be delayed by low levels of early childhood stimulation (1,3). In the Peruvian Amazon there is a high prevalence of various risk factors associated with developmental delay, especially in rural areas. A study conducted in 2017 showed that the prevalence of developmental delay in the Amazon of Peru was 26.7% (4). In the Amazonian

department of Loreto, the prevalence of childhood anemia is 49.9% and chronic malnutrition is 23.6% (2017) (5). Those indicators are worse in indigenous communities (6–9).

The well-being of children in communities can be greatly increased by improving families' understanding of healthy child-rearing practices. Health promotion strategies that establish an intercultural dialogue with families do a better job at promoting healthy practices (10,11). A program can train and support community members to conduct health promotion that can create behavior changes and improve child development outcomes. Community Health Agents (CHAs) can play an essential role in reducing inequalities in health services by acting as a link between communities and the local health services (11–13). The CHA can establish a warm relationship with the caregiver, thus increasing the acceptance of health advice, improving the absorption of knowledge and getting caregivers involved in the identification and resolution of their own health problems (14–21). The positive impact of CHAs has been associated with a reduction in malnutrition, anemia, malaria, cases of diarrhea, improved child development, and other health indicators (11,22,23). Therefore, understanding and improving the performance of CHAs can greatly improve behavioral outcomes of caregivers, increase the utilization of local health services, and enhance the overall health and well-being of communities (14,24–31).

Several studies have shown that a mobile information and communication technology (ICT) can improve the performance of CHAs in their ability to perform health promotion, collect and report timely information regarding family health, provide health services such as vaccines, and refer families to appropriate local health services (32–39). Additionally, when a mobile ICT tool is used by a CHA, the device can increase the confidence the caregivers have in the messages being transmitted and increase the confidence the CHAs have in their own work (32,33,37,38,40,41). Through implementation science, innovations in mobile ICTs and strategies for child health and development can be extended to low resource settings to empower local actors and spread the benefits of advancements in technology (35,36).

A study on the performance of CHAs in the Peruvian Amazon identified difficulties they face in their work. They had difficulty providing a clear explanation of the causes of common diseases, remembering essential steps of home visits, and diversifying the health topics that were discussed (29). As described above, an mHealth tool could help the CHAs overcome some of the difficulties they have in conducting an effective home visit. However, there is currently little evidence on the impact of an mHealth tool when used as an educational device by CHAs to improve child development (33). Additionally, there is a knowledge gap on the impact that an mHealth tool can have when utilized by CHAs in rural regions of Peru. Therefore, the present study aims to demonstrate the impact of an mHealth tool used for health promotion and surveillance by CHAs to improve child development in the Peruvian Amazon.

4. HYPOTHESIS

The study hypothesizes that an mHealth tool and digital educational content developed for the local context will improve the capacity of the CHAs to transmit health messages to the caretakers, thus creating behavior change that will lead to better health and child development for the children. The hypothesis is based on a theory of change that considers the potential outputs and outcomes that are expected occur as a result of the intervention (42). The theory of change displayed in Figure 1 highlights the various components that are included in the tablet-based application and unfolds the expected outcomes of each. The theory of change is presented as a comparison to the status-quo; traditional CHA programs in Peru that use paper-based reporting and educational material.

Based on the Theory of Change, the study has the following hypotheses:

H1: The mHealth tool will improve the performance of CHAs during their home visits with children, as measured by doses, content, and inter-personal relationships.

H2: Improved performance by CHAs will increase knowledge acquisition and healthy child-rearing practices by caregivers.

H3: Improved knowledge and healthy practices by caregivers will improve the health and development of the children that receive the intervention.

5. OBJECTIVES

5.1. Main Aim

The objective of the study is to evaluate the impact of the mHealth tool (tablet with application) on child development and nutrition status of children aged 6 to 36 months compared to children who receive home visits from CHA without the mHealth tool.

5.2. Primary Outcomes

1. *[Primary Objective]* Improve child development scores for the children in the intervention group in the domains of language, cognition, gross motor, and social-emotional by 20% compared to the children in the control group ($p<0.05$).
2. Decrease the prevalence of anemia in children by 20% compared to the baseline measurement.
    a. Children in the intervention group will experience a greater reduction in the prevalence of anemia than children in the control group ($p <0.05$)
3. Decrease the prevalence of chronic malnutrition in children by 15%, compared to the baseline measurement.
    a. Children in the intervention group will experience a greater reduction in the prevalence of chronic malnutrition than children in the control group ($p <0.05$).

5.3. Secondary Outcomes

The secondary outcomes of the intervention include indicators of behavior change by CHA and families that have established causal connections with improved health and child development. The intervention is expected to achieve the following secondary outcomes:

4. The caregivers of the intervention group will improve knowledge evaluation scores by 50% compared to the baseline measurement.
5. CHAs in the intervention group will improve their performance evaluation scores by 50% compared to the baseline measurement.
6. More than 50% of the CHAs in the intervention group will express improved satisfaction and self-efficacy when compared to the baseline data.
7. The caregivers of the intervention group will use the local health services for children's health more frequently than they did during the baseline.

6. METHODS

6.1. Study Design

The impact will be evaluated through an experimental cluster randomized controlled trial. Each cluster represents a CHA because the children that receive visits from the same CHA must receive the same intervention. Each cluster will be matched with a second cluster using covariate-constrained randomization (43). Recruitment and baseline surveys will be conducted before allocation to the intervention or control group for each cluster. The variables that will be used to

covariate-constrained randomization include: the size of the community, type of health facility in the community, and distance to the nearest health center (level I-2), and prevalence of anemia. For each cluster pair, one cluster will be randomly assigned to the intervention group and the other to the control group. The covariate-constrained randomization will be conducted with an open-sourced algorithm and the program, R (44).

6.2. **Location**

The study will be implemented in the Amazon region of Peru. The study will be carried out in the department of Loreto, province of Maynas, and districts of Mazan, Punchana, and Indiana. The district of Mazan has a population of 13,779 (45), a prevalence of chronic malnutrition of 24.4% and a prevalence of anemia at 39.1%, in 2017 (46). The capital of the district of Mazan is located approximately one and a half hours by boat from the capitol city of the province, Iquitos. The district of Punchana has a population of 91,128 (45), a prevalence of chronic malnutrition of 22.7% and a prevalence of anemia of 39.9% (46). The capital of Punchana, is 20 minutes from the city of Iquitos. The district of Indiana has a population of 11,301 (45), a prevalence of chronic malnutrition of 22.4%, and a prevalence of anemia at 46.7%, in 2017(46). The capital of the district to Indiana is 1.5 hours by boat from the city of Iquitos.

The research team with the support of the Regional Ministry of Health of Loreto, will choose the communities that will be included in the study after traveling to the communities to ensure they meet the selection criteria. The study communities must have the following characteristics:

- Has an active CHA that visits families in their community.
- Is not a participant in another health related study.
- Is located less than 6 hours from Iquitos.
- Has at least 25 families and a maximum of 1500 families.

The communities must have an active CHA program for the study to be because we are measuring the impact of included the mHealth tool in existing CHA programs. The community cannot be participating in another study that includes an intervention that was/will be implemented due to the confounding variables that would cause in our study and the other study. The communities must be less than 6 hours from Iquitos due to budgetary restraints that hinder the research team's ability to consistently travel 6 or more hours to execute the study. The size limitation of the community is required to ensure the study obtains a minimum number of children that are reached per tablet/CHA.

6.3. **Participants and Sample Size**

The study population includes:

- 10-14 communities, half in the intervention group and half in the control group.
- 40-50 CHAs, half CHAs in the intervention group and half CHAs in the control group.
- 400-450 children, half in the intervention group and one half in the control group

All children between 0 - 36 months in the communities will receive visits from a CHA, in the intervention and control group. However, only the CHAs in the intervention group will receive a tablet with the application to assist their home visits. All the children in the intervention group will have the opportunity to receive the intervention with the tablet.

To assess the impact of the intervention, a sample of the population will be chosen at random to receive the evaluation. The inclusion criteria for the study sample are the following:

- Children who belong to one of the communities included in the study, aged 6 to 36 months.
- Primary caregiver of the child is older than 15 years.
- The caregiver is willing to receive visits from the CHA.

The minimum age of children to be included in the impact evaluation is determined by the quality of the early childhood development tools. Assessment of child development is more accurate with children older than 5 months (47). The maximum age of the children for the study is determined by the CHA program, which limits home visits by CHAs to children up to 36 months old. The minimum age of the caregiver is 16 because that is the age determined by the communities and the local ethics committee to be capable of giving an informed consent. It is important to capture information from mothers below 18 years old because 39% of the mothers in the region have their first child before the age of 17 (4). Caregivers that do not want to receive visits from CHAs will be excluded because they will not receive the intervention, nor be included in the control group.

The exclusion criteria for the study sample are:

- Families where the main caregiver or the child does not speak Spanish.
- Families that do not want to receive home visits from CHAs.
- Children with mental or physical disabilities.

Families that do not speak Spanish cannot be included because the study does not have appropriate translators for indigenous languages. Children with disabilities will be excluded in the evaluation because the child development evaluation tool is not equipped to evaluate children with these conditions. However, children with disabilities will still receive the intervention.

The sample size for the evaluation is calculated to measure the effect size on the primary outcome indicator, child development. A study in the Amazon region of Peru (2017) determined that the standard deviation of communication scores, determined by the Ages and Stages Questionnaire, was 15.19 (4). The current study predicts a 20% increase in child development scores, which will result in an effect size of 0.49 (average communication score was 37.48, a 20% increase is 44.98, 0.49 standard deviations) (data available in public repository) (4). To calculate the minimal sample size needed, the following parameters were determined:

- Two-sided significance level: 0.05
- Power: 90%
- Effect Size: 0.49
- Avg. Cluster Size: 9
- Intra Cluster Correlation (ICC): 0.15
- Variance Inflation Factor (VIF): 2.2

The following calculation is used to determine the sample size:

$$N \text{ per group} = \frac{[(z_{alpha} + z_{beta})^2 \times 2 \times SD^2]}{\text{Expt'd diff}^2} = \frac{(1.96 + 1.28)^2 \times 2 \times 15.19^2}{(15.19 \times .49)^2}$$

The sample size per group (t-test) with no clusters would be 86. To control for the Intra-Cluster Correlation (ICC), the per group sample size (86) is multiplied by the Variance Inflation Factor (VIF=1+(Avg. Cluster Size–1)*ICC=2.2) to determine the minimal sample size to be **189 per group** (48). The study will include 21 clusters and 9 children and caregivers per cluster.

6.4. **Instruments**

To measure the impact of the intervention and understand the perspective of the users, a series of instruments will be applied to the study participants. The instruments include; evaluation of child development, attitudes and practices questionnaire, knowledge evaluation, performance evaluation of CHAs, and collection of anemia and anthropometric indicators. Qualitative surveys will also be used to evaluate the satisfaction of CHAs and caregivers in relation to the intervention.

The questionnaires and evaluations will be carried out in the homes of the participants. The researcher will ask if a caregiver of a child within the age range is in the home, if so they will explain the study and ask the caregiver if they want to participant and are willing to sign the informed consent. The researcher will record the responses of the questionnaires and evaluation on a smart phone or electronic tablet.

6.4.1. Evaluation of Child Development

Child development can be effectively evaluated with an instrument that utilizes caregiver-reported data to assess the ability of the child to perform age-relevant developmental activities (47,49–52). The current study will use the Caregiver-Reported Early Development Instrument (CREDI) to evaluate child development (53,54). The CREDI has been validated as an effective instrument to evaluate child development, including low-resource settings in 17 countries (54). The CREDI is effective for large-scale, population-wide studies because it requires less time, materials, and evaluator expertise than other similar instruments (53).

The CREDI is conducted by asking the caregiver if the child is currently capable of completing a list of age-appropriate activities, in which the caregiver can respond by indicating; yes, no, or I don't know. The CREDI will provide a developmental score and a classification that represents the child's development trajectory as; normal development or at risk of developmental delay. These classifications will be used as the primary dependent variables of the study.

6.4.2. Attitudes and Practices Questionnaire

The study will use a quantitative questionnaire to measure the attitudes and practices of caregivers that influence maternal and child health. The following topics are included in the questionnaire: demographic information, safe pregnancy practices, feeding practices, prevention of illnesses, early childhood stimulation, and use of local health services. The questionnaire will be conducted with all caregivers of the children included in the study. The questionnaire will take approximately 10 minutes.

6.4.3. Knowledge Evaluation

To assess the knowledge of caregivers of healthy practices for maternal and child health, an instrument was built based on the literature (13,55–57). The Knowledge Evaluation asks the caregiver questions regarding maternal and child health, nutrition, sanitation, and infectious diseases. The questions are open-ended to give the caregiver the opportunity to provide multiple answers that displays their knowledge of the topic.

The Knowledge Evaluation will take place directly after the Attitudes and Practices Questionnaire. The Knowledge Evaluation will be scored by giving the participant 1 point for every correct answer they provide. The correct answers will be added together to provide a total "Knowledge Score" for the caregiver.

6.4.4. Performance Evaluation of CHAs

The Performance Evaluation of CHAs was based on an instrument built by the University of West Indies and the Inter-American Development Bank to measure the quality of home visits by CHAs (14). The Performance Evaluation includes questions related to the use of materials, activities, promotion of child development, relationship between CHA and caregivers, and relationships between the CHA and the child. The Performance Evaluation was modified and validated during a previous study in the Amazon region within the local CHA program. The instrument provides further focus on health messages provided by the CHA and the needs of the communities in the Amazon (29).

The conduct the performance evaluation, the researcher will accompany the CHA on their home visit with a child to observe the home visit. The researcher will observe the home visit in silence, trying not to influence the dynamic of the visit. The researcher will take notes during the visit and complete the Performance Evaluation immediately after the conclusion of the home visit.

6.4.5. Survey of the Use of Local Health Services

The research team will survey the local health centers in the communities to obtain statistics regarding the use of health services related to maternal and child health, including: child growth monitoring check-ups, prenatal check-ups, immunization coverage, distribution of micronutrient supplements, distribution of anti-parasitic medicine, and distribution of oral rehydration salts for diarrhea. The survey will be conducted with the nurse that conducts maternal and child health evaluations at the health center. The survey will take approximately 15 minutes and can be filled out independently by the health post representative.

6.4.6. Survey of Child Health Indicators

The CHEST application will be used to collect child health indicators by CHAs during their home visits. The children have a card with information that was recorded during their growth monitoring check-ups at the local health center, including height, weight, age, vaccines, and hemoglobin levels (when tested). The CHA will observe the information written on the card and record it with the CHEST application. The CHA will also ask additional questions regarding the health of the child, including incidences of diarrhea, cough, fever, malaria and other illness. The data from the application will be uploaded to the secured server when the CHA or supervisor has access to the cellular network.

6.4.7. Questionnaire on Satisfaction and Self-Efficacy of CHAs

The Questionnaire on Satisfaction and Self-Efficacy of CHAs will be used to measure the degree satisfaction and self-efficacy the CHAs have from using the CHEST application during their home visits. The questions are both quantitative and qualitative. The CHAs will have the opportunity to describe how the experience with the tablet could be improved.

6.4.8. Questionnaire on Satisfaction of Caregiver

The Questionnaire on Satisfaction of caregivers will be used to measure the degree satisfaction of the caregivers that received the intervention. The questions are both quantitative and qualitative. The caregivers will have the opportunity to describe what they like and don't like about the use of a tablet during the home visits.

6.5. **Patient and Public Involvement**

The study was created through formative research done in the same communities to identify their needs and desires related to improving child health and development. A performance evaluation study was conducted with the CHAs in the region by the author (29). In the study, the CHAs and

caregivers expressed their need and desire for more information regarding topics of health and child development. The current intervention was created to address those needs.

The results of the study will be presented to the participants, including the community health agents, caregivers, health facility personal, and Regional Ministry of Health in the form of a study brief that indicates the results of each indicator collected. The results will be presented to the public via publication of results in an international scientific journal.

Patients were not involved in the design or recruitment of the study.

7. INTERVENTION

The intervention includes the development and implementation of a tablet-based application (CHEST) to improve the performance of the CHAs during their home visits. The CHAs will use the CHEST Application during their home visits to teach caregivers good health practices and early childhood stimulation. The application will provide the steps for the CHA to follow to conduct an effective home visit. The application will include videos and images to show the caregiver to transmit key health messages. Also, the application will organize the case load of children of the CHA and will provide a mechanism to record maternal and child health indicators.

The intervention is described in the following five phases:

7.1. **Phase 1: Preparation of Material**

7.1.1. Step-by-Step Agendas for Home Visits

The research team will work with the Regional Ministry of Health of Loreto to build agendas for home visits by the CHAs. The health messages for the home visits are based on national and international manuals for home visits by CHAs to teach maternal and child health and development (58–61). The agendas include steps to follow by the CHA to provide a quality home visit and collect child health indicators. The messages included in the agendas include; what nutritious foods should be consumed by children, how to avoid diarrhea and other diseases, good practices of early attention, and use of health services. There will be 1 agenda for each month of age of the child (1-36 months).

7.1.2. Multimedia Material

The research team will generate multimedia material to be used in the application to transmit health messages. The content will be designed to convey the health messages clearly within the local culture in the Amazon. The material will include videos of people from the region acting out health topics, instructional videos on early childhood stimulation, and animations that describes health issues. In addition, the application will include educational images that have been developed by the regional Ministry of Health of Loreto and other institutions.

7.2. **Phase 2: Development of the Application**

The research team will evaluate the mHealth applications that have been developed and are open source to determine which will be best to adapt for the current project. The project will contract a team of program developers to modify the open source application to fit the current objectives and local context. The program developer will include the agendas, multimedia, and data collection mechanisms in the application. The application will function without internet signal and protect all information by password.

7.3. **Phase 3: Baseline Data Collection**

The research team will conduct the surveys and evaluations in the intervention and control communities to obtain a baseline for the study. The instruments that will be applied for the baseline survey include the *Child Development Evaluation, Attitudes and Practices Questionnaire, Knowledge Evaluation, Performance Evaluation of CHA, and Survey on the Use of Health Services*. The baseline survey will be completed before implementation beings in the intervention and control communities.

7.4. **Phase 4: Implementation of Intervention**

7.4.1. Training Workshops

The research team will conduct training workshops with the CHAs in the intervention group to teach them how to use the tablet and application. The workshops will occur during a period of 3 days, 4 hours per day. The leaders of the health facility and Regional Ministry of Health of Loreto will be invited to participate in the workshops and in the supervision of the development of the project.

7.4.2. Distribution of Tablets

After the training workshops, the research team will give a tablet to each CHA in the intervention communities. The CHAs will be instructed to bring the tablet to local health center if they are having problems with the tablet or to store the tablet in their home until a member of the monitoring team visits their community. A supervisor of the CHA program will visit the CHAs to ensure the App is being used and functioning correctly.

7.4.3. The Intervention

The CHAs will continue to conduct home visits with the children in their caseload the same as before the distribution of the tablets. The only change is that the CHAs will use the tablets during the home visits. The number of home visits depends on the demands placed by the community and the motivation of the individual CHA. The CHAs in the communities typically conduct 1-4 home visits per month with children aged 0-36 months. The CHAs are instructed to teach the caregivers good sanitation, nutrition, and child development practices.

The CHAs will use the tablet-based app to visualize the health indicators of the children in their caseload, record health indicators of the child during each visit, observe and chare images and videos that will help teach health and development messaging, and send data to a central database. The App will guide the CHA through each step of the home visit. The supervisor of the CHA program will visit the CHAs to ensure they can upload their data to the database. This include, in some cases, carrying the tablet to a community that has signal to upload the data.

7.4.4. Monitoring

The research team will supervise the work of the CHAs through observations of their home visits and interviews with families and CHAs in the communities. The research team will visit the communities every month during the first 4 months, and less frequently when they see that the program is working as it should.

The team will also track activities of the CHAs through the data uploaded by the application. They will be able to track the number of visits being conducted and the health indicators of the children. If the tablet is not uploading data to the survey, the research team will visit the community to identify the problem.

The local health facility will also have access to the data and will be able to identify if a child is at risk of chronic malnutrition, chronic diarrhea and/or is not attending growth monitoring check-ups.

7.5. **Phase 5: Evaluation of the Intervention**

At the end of the intervention, the follow-up survey will be carried out in the intervention and control communities. The instruments included in the follow-up survey include the *Evaluation of Child Development, Attitudes and Practices Questionnaire, Knowledge Test, Performance Evaluation of CHA, Survey of Use of Health Services, Questionnaire on Satisfaction and Self-Efficacy of CHA*, and *Questionnaire on Satisfaction of Caregivers*.

The data gathered by the application will be used to evaluate the child heath indicators and the number of home visits conducted.

8. DATA ANALYSIS

The quantitative data obtained in the surveys will be organized and analyzed with the statistical software, Epi Info version 7.1.4.0 (62). The qualitative data will be organized and analyzed with the program Atlas.ti (63). To carry out the impact analysis, four mathematical models will be used to interpret the results, generating an optimal analysis to understand the interactions between the variables. First, a descriptive analysis will be performed to compare indicators between the analysis groups, including average and frequencies of the independent and dependent variables. Second, a bivariate analysis with Chi-square test will be done to examine the associations between the independent and the dependent variables. Third, a multivariate regression analysis will be used to examine the interactions between the independent variables and the dependent variables. Fourth, an analysis of covariance (ANCOVA) regression method will be used to calculate the impact of the intervention (43).

The secondary outcomes will be evaluated by comparing the indicators measured during the follow-up survey with the indicators measured during the baseline survey using descriptive statistics. The indicators will be compared by their average scores and frequency.

8.1. **Data Monitoring**

Data monitoring will be completed by the Data Monitoring Committee to ensure non-biased handling and analysis of data obtained from baseline, monitoring, and follow-survey. The Data Monitoring Committee will be made up of the team of experts that will be hired to create the content of the intervention and mentors that guided the research team. The Data Monitoring Committee will each guard files of data at different time points so they can later be crossed reference to ensure consistency. The Data Monitoring Committee will not include permanent members of the sponsor organization or associates of the funding organization or anyone with competing interest or incentive for the intervention to be successful.

8.1. **Data security**

All data will be stored in a secure encrypted server that is protected by password. All identifiable information in the data set will be deleted to make it impossible to link the data with the individual. Information regarding contact information of CHAs will be stored on the secure server. There will be no need to maintain identifies within the data because there will be no follow-up serves with individuals. Members of the Data Monitoring Committee will ensure all identifiable information has been removed from the data set.

9. ETHICAL CONSIDERATIONS

The investigation was approved by the Ethics Committee of the National Hospital "San Bartolomé" on November 8, 2018 (Exp. Number 15463-18, Oficio N. 0744-2018-OADI-HONADOMANI-SB)

The investigation will include only those individuals that are willing and able to give their consent to be included in the study. The participant must be able to understand the information presented to them and voluntarily express their choice of whether they want to participate or not. The caregivers must be over 15 years of age to participate in the study.

It will be clearly stated that participation in the study will not compromise the health of the participants or violate any rights of the child. There will be no financial compensation for participation in the study. No biological samples will be collected, nor any medical or pharmacological treatments delivered in the research process. There are no possible adverse effects associated with participation in the study. There is the possibility of generating discomfort in the participants because the visits and surveys imply an investment of time. Given this, participants will be informed about the amount of time involved for their participation in the survey before signing the informed consent.

After completion of the child development evaluation the results will be immediately shared with the caretaker along with recommendations of early childhood stimulation activities that could benefit the child. Likewise, the results of the evaluations will be communicated to the health center of the community with a copy of a list of the children who are at risk of developmental delay. The child development evaluation represents a direct benefit to the participants in the intervention and control group.

The research team will monitor the intervention for the at least 12 months to ensure the CHAs receive support, and the tablets receive maintenance or are replaced if need. The CHAs will also have the opportunity to opt-out of the intervention at any time, thus returning to their traditional methods of reporting and health promotion. After 12 months, the program will be handed over to the appropriate local government agency, but continue to provide support as needed.

The results obtained from the study will be made publicly accessible through the publication of finding and a report delivered to the local health authorities. The dataset will available in a public data repository.

9.1. **Informed consent for caregivers**

The Informed Consent for Caregivers includes the description of the study, the participation of the caregiver, the participation of the child, and the amount of time required to complete the survey. The interviewer that conducts the questionnaires will ask for consent from the caregiver. If the caregiver agrees to participate in the study, they will be asked to sign the Informed Consent form. The caregiver will be provided a copy of the consent.

9.2. **Informed consent for CHA**

The Informed Consent for CHAs includes a description of the study and the performance evaluation that will be conducted with the CHA. The interviewer that conducts the questionnaires will ask for consent from the CHA. If the CHA agrees to participate in the study, they will be asked to sign the Informed Consent for CHAs. The CHA will be offered a copy of the consent.

9.1. **Consent to Publish**

There will be no identifying images, personal details, or clinical details of participants presented that will compromise the anonymity of the participants in the study.

10.CONCLUSIONS

The results of the study will provide evidence on the potential of a mHealth tool to improve child health and development indicators in the region. The process evaluation with qualitative assessments will also be conducted to identify barriers, strengths, and weaknesses of the program.

11.ABBREVIATIONS

CHA – community health agents
CHEST – Child Health Education and Surveillance Tool
CREDI – Caregiver-Reported Early Development Instrument
ICT – Information and communication technology

12. DECLARATIONS

12.1. Availability of data and materials

The datasets generated during and analysed during the current study will be stored in the publically available repository, figshare (https://figshare.com/). De-identified participant data, including child development evaluation scores, anemia results, chronic malnutrition results, KAP survey results, and CHA performance evaluations, will be stored in the repository. The data will be available through the repository for 10 years. Data from participants will only be made available if consent was provided by the participant through the informed consent process.

12.2. Competing interests

The authors and members of the research team have no competing interest.

12.3. Communication of Trail Results

The results of the study will be presented to the participants, including the community health agents, caregivers, health facility personal, and Regional Ministry of Health in the form of a study brief that indicates the results of each indicator collected. The study brief will be written and described in a manner that is intelligible for the target population. The CHAs will be asked to distribute the brief and describe the findings to the individual families in their caseload.

The results will be presented to the public via publication of results in an international scientific journal. The research team will also seek opportunities to present the results in national and international conferences to disseminate findings.

12.4. FUNDING

The study is funded by the grant, Saving Brains, by Grand Challenges, Canada. The funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

12.5. AUTHOR CONTRIBUTIONS

CW conceived of the study. CW and NR contributed to the writing and revision of the protocol. PM provided advisory on study design. All authors contributed to refinement of the study protocol and approved the final manuscript.

12.6. **ACKNOWEDGEMENTS**

Special thanks to Liz Franco, Luis Orrego Ferreyros, Milagros Alvarado Llatance, and Gabriela Palacios Rojo for their assistance in developing the material and instruments of the study. Thanks to the Ministry of Development and Social Inclusion of Peru for their collaboration in designing the tool and identifying the participants and recipients of the study. Special thanks to Grand Challenges Canada for providing advisory service regarding study design, implementation strategies, and strategies to scale the intervention.

13.CHRONOLOGY

The study will last 24 months, beginning in October 2018 and ending in September 2020. The schedule of activities can be found in Table 1.

Table 1: Schedule of Activities

Activity	Oct	Nov	Dec	Jan '19	Feb	Mar	Apr	May	June	July-August	Sep-Dec	Jan-April '20	May-Aug '20
Complete Ethics Committee Protocol	■	■	■										
Develop home visit agendas			■	■	■	■	■	■					
Validate home visit material						■	■	■	■				
Create videos					■	■	■	■					
Develop Application		■	■	■	■	■	■	■					
Validate Application							■	■	■				
Recruit participants								■	■				
Baseline Survey								■	■				
Train CHAs									■				
Deploy App									■	■	■	■	■
Monitoring									■	■	■	■	■
Final Evaluation													■
End of Project													■

13.1. Flow Diagram schedule of activities

The Flow Diagram in Table 2 describes when intervention allocation and assessments of the study population will take place, in relation to the study activities.

Table 2: Flow Diagram

	Study Period				
	Enrolment	**Allocation**	***Post-Allocation***		***Close-out***
TIMEPOINT	$-t_1$	**0**	t_1	t_2	t_x
ENROLMENT:					
Eligibility screen of inclusion and exclusion criteria	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
Distribution of Tablet			◆—	—	—◆
Control group			◆—	—	—◆
ASSESSMENTS:					

Child development evaluation	X				X
Performance Evaluation	X				X
Knowledge, Attitudes, and Practices Survey	X				X
Monitoring of Community Health Agents		X	X	X	

14.TRAIL SPONSOR

Trail Sponsor: Elementos
Contact Name: Christopher Westgard
Address: Jiron Domeyer, Barranco, Lima, Peru
Telephone: +51927980400
Email: cmwestgard@gmail.com

15. REFERENCES

1. Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B. Developmental potential in the first 5 years for children in developing countries. The Lancet. 2007 Jan 6;369(9555):60–70.

2. Engle PL, Black MM, Behrman JR, Mello MC de, Gertler PJ, Kapiriri L, et al. Strategies to avoid the loss of developmental potential in more than 200 million children in the developing world. The Lancet. 2007 Jan 20;369(9557):229–42.

3. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. Lancet Lond Engl. 2011 Oct 8;378(9799):1325–38.

4. Westgard C, Alnasser Y. Developmental delay in the Amazon: The social determinants and prevalence among rural communities in Peru. PloS One. 2017;12(10):e0186263.

5. Instituto Nacional de Estadistica e Informatica. Loreto Compendio Estadistico 2017. Sistema Estadistico Nacional; 2017.

6. Anticona C, San Sebastian M. Anemia and malnutrition in indigenous children and adolescents of the Peruvian Amazon in a context of lead exposure: a cross-sectional study. Glob Health Action. 2014;7:22888.

7. Díaz A, Arana A, Vargas-Machuca R, Antiporta D. Situación de salud y nutrición de niños indígenas y niños no indígenas de la Amazonia peruana. US11 [Internet]. 2015 [cited 2017 Jan 26]; Available from: http://iris.paho.org/xmlui/handle/123456789/10008

8. Flores-Bendezu J, Calderon J, Rojas B, Alarcon-Matutti E, Gutierrez C. Chronic malnutrition and anemia in children under 5 years of indigenous households of Peru - Analysis of Demographic and Health Survey 2013. Fac Med 2015762135-40 Dxdoiorg1015381analesv76i211139.

9. Grantham-McGregor SM, Fernald LCH, Kagawa RMC, Walker S. Effects of integrated child development and nutrition interventions on child development and nutritional status. Ann N Y Acad Sci. 2014 Jan;1308:11–32.

10. Perry HB, Sacks E, Schleiff M, Kumapley R, Gupta S, Rassekh BM, et al. Comprehensive review of the evidence regarding the effectiveness of community–based primary health care in improving maternal, neonatal and child health: 6. strategies used by effective projects. J Glob Health [Internet]. [cited 2017 Nov 9];7(1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5491945/

11. Gilmore B, McAuliffe E. Effectiveness of community health workers delivering preventive interventions for maternal and child health in low- and middle-income countries: a systematic review. BMC Public Health. 2013 Sep 13;13:847.

12. Global Health Workforce Alliance, World Health Organization. Global experience of community health workers for delivery of health related millennium development goals: a systematic review, country case studies, and recommendations for integration into national health systems. 2010.

13. The Earth Institute. Millennium Villages Project. Community Health Worker Trainer's Manual. A guide to Home Based Services [Internet]. Version 2.1. Columbia University; 2013. Available from: http://millenniumvillages.org/wp-content/uploads/2014/09/CHWTrainingManual.pdf

14. Leer J, Lopez-Boo F, Perez Exposito A, Powell C. A Snapshot on the Quality of Seven Home Visit Parenting Programs in Latin America and the Caribbean. Inter-American Development Bank; 2016.

15. Schodt S, Parr J, Maria CA, Rubio-Codina M. La medición de la calidad de os servicios de visitas domiciliarias . Una revisión de la literatura. Danco Interamericano de Desarrollo; 2015.

16. Vogel CA, Caronongan P, Thomas J, Bandel E, Xue Y, Henke J, et al. Toddlers in Early Head Start: A Portrait of 2-Year-Olds, Their Families, and the Programs Serving Them. Volume 1: Age 2 Report. OPRE Report 2015-10 [Internet]. Administration for Children & Families; 2015 [cited 2017 Aug 3]. Available from: https://eric.ed.gov/?id=ED558558

17. Roggman LA, Cook GA, Innocenti MS, Jump Norman V, Boyce LK, Christiansen K, et al. Home Visit Quality Variations in Two Early Head Start Programs in Relation to Parenting and Child Vocabulary Outcomes. Infant Ment Health J. 2016 May 1;37(3):193–207.

18. Medina A, Sofía I. Evaluation protocol application of tasks for the socio - cognitive development in children from 37 to 71 months in the Program of Comprehensive Attention to Early Childhood Modality Family Environment District Secretariat of Social Integration [Internet]. [cited 2017 Aug 3]. Available from: https://intellectum.unisabana.edu.co/handle/10818/23587

19. Fernández S, Yonah R. Aplicación de ensayos domiciliarios para evaluar la adopción de prácticas mejoradas de alimentación complementaria en madres. Centro materno infantil Juan Pablo II. Villa El Salvador, Lima. 2005. Univ Nac Mayor San Marcos [Internet]. 2007 [cited 2017 Aug 4]; Available from: http://cybertesis.unmsm.edu.pe/handle/cybertesis/1121

20. Walker SP, Powell C, Chang SM, Baker-Henningham H, Grantham-McGregor S, Vera-Hernandez M, et al. Estrategias de apoyo parental a través de los servicios de salud en el Caribe [Internet]. BID; 2016 Feb [cited 2017 Aug 3]. Available from: http://repositorio.minedu.gob.pe/handle/123456789/4112

21. Chang-Say Chong A. La comunicación en los proyectos de lucha contra la desnutrición crónica infantil : el caso Ally Micuy (Áncash). Pontif Univ Católica Perú [Internet]. 2014 Sep 25 [cited 2017 Aug 3]; Available from: http://tesis.pucp.edu.pe/repositorio/handle/123456789/5598

22. Lewin S, Munabi-Babigumira S, Glenton C, Daniels K, Bosch-Capblanch X, Wyk BE van, et al. Lay health workers in primary and community health care for maternal and child health and the management of infectious diseases. Cochrane Database Syst Rev [Internet]. 2010 [cited 2018 Sep 19];(3). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004015.pub3/abstract

23. Lassi ZS, Kumar R, Bhutta ZA. Community-Based Care to Improve Maternal, Newborn, and Child Health. In: Black RE, Laxminarayan R, Temmerman M, Walker N, editors. Reproductive, Maternal, Newborn, and Child Health: Disease Control Priorities, Third Edition (Volume 2) [Internet]. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2016 [cited 2016 Jun 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK361898/

24. Howard KS, Brooks-Gunn J. The role of home-visiting programs in preventing child abuse and neglect. Future Child. 2009;19(2):119–46.

25. Singh V, Ahmed S, Dreyfuss ML, Kiran U, Chaudhery DN, Srivastava VK, et al. Non-governmental organization facilitation of a community-based nutrition and health program: Effect on program exposure and associated infant feeding practices in rural India. PloS One. 2017;12(9):e0183316.

26. Swider SM. Outcome Effectiveness of Community Health Workers: An Integrative Literature Review. Public Health Nurs. 2002 Jan 1;19(1):11–20.

27. Agarwal S, Perry HB, Long L-A, Labrique AB. Evidence on feasibility and effective use of mHealth strategies by frontline health workers in developing countries: systematic review. Trop Med Int Health TM IH. 2015 Aug;20(8):1003–14.

28. Mobile Healthcare Information for All. Assessment of mHealth applicaitons for their potential to provide essential healthcare information for citizens in low resource settings. HIFA; 2017.

29. Westgard C, Naraine R, Paucar Villacorta DM. Performance Evaluation of Community Health Workers: Case Study in the Amazon of Peru. J Community Health. 2018 Mar 26;

30. Ballard M, Montgomery P. Systematic review of interventions for improving the performance of community health workers in low-income and middle-income countries. BMJ Open. 2017 Oct 1;7(10):e014216.

31. Cometto G, Ford N, Pfaffman-Zambruni J, Akl EA, Lehmann U, McPake B, et al. Health policy and system support to optimise community health worker programmes: an abridged WHO guideline. Lancet Glob Health. 2018 Dec 1;6(12):e1397–404.

32. Ilozumba O, Dieleman M, Kraamwinkel N, Belle SV, Chaudoury M, Broerse JEW. "I am not telling. The mobile is telling": Factors influencing the outcomes of a community health worker mHealth intervention in India. PLOS ONE. 2018 Mar 27;13(3):e0194927.

33. van Heerden A, Sen D, Desmond C, Louw J, Richter L. App-Supported Promotion of Child Growth and Development by Community Health Workers in Kenya: Feasibility and Acceptability Study. JMIR MHealth UHealth [Internet]. 2017 Dec 5 [cited 2018 Sep 19];5(12). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5736876/

34. Lee S, Chib A, Kim J-N. Midwives' Cell Phone Use and Health Knowledge in Rural Communities. J Health Commun. 2011 Oct 1;16(9):1006–23.

35. Peterson HB, Haidar J, Fixsen D, Ramaswamy R, Weiner BJ, Leatherman S. Implementing Innovations in Global Women's, Children's, and Adolescents' Health: Realizing the Potential for Implementation Science. Obstet Gynecol. 2018 Mar;131(3):423–30.

36. Peterson HB, Haidar J, Merialdi M, Say L, Gülmezoglu AM, Fajans PJ, et al. Preventing maternal and newborn deaths globally: using innovation and science to address challenges in implementing life-saving interventions. Obstet Gynecol. 2012 Sep;120(3):636–42.

37. Källander K, Tibenderana JK, Akpogheneta OJ, Strachan DL, Hill Z, Asbroek AHA ten, et al. Mobile Health (mHealth) Approaches and Lessons for Increased Performance and Retention of Community Health Workers in Low- and Middle-Income Countries: A Review. J Med Internet Res. 2013;15(1):e17.

38. Prinja S, Nimesh R, Gupta A, Bahuguna P, Gupta M, Thakur JS. Impact of m-health application used by community health volunteers on improving utilisation of maternal, new-born and child health care services in a rural area of Uttar Pradesh, India. Trop Med Int Health TM IH. 2017;22(7):895–907.

39. Ilozumba O, Van Belle S, Dieleman M, Liem L, Choudhury M, Broerse JEW. The Effect of a Community Health Worker Utilized Mobile Health Application on Maternal Health Knowledge and Behavior: A Quasi-Experimental Study. Front Public Health [Internet]. 2018 May 7 [cited 2019 Apr 30];6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5949315/

40. Chib A. The Aceh Besar midwives with mobile phones project: Design and evaluation perspectives using the information and communication technologies for healthcare development model. J Comput-Mediat Commun. 2010 Apr 1;15(3):500–25.

41. Limaye NP, Rivas-Nieto AC, Carcamo CP, Blas MM. Nuestras Historias- Designing a novel digital story intervention through participatory methods to improve maternal and child health in the Peruvian Amazon. PLOS ONE. 2018 Nov 5;13(11):e0205673.

42. Lafferty CK, Mahoney CA. A Framework for Evaluating Comprehensive Community Initiatives. Health Promot Pract. 2003 Jan 1;4(1):31–44.

43. Ivers NM, Halperin IJ, Barnsley J, Grimshaw JM, Shah BR, Tu K, et al. Allocation techniques for balance at baseline in cluster randomized trials: a methodological review. Trials. 2012 Aug 1;13(1):120.

44. Carter BR, Hood K. Balance algorithm for cluster randomized trials. BMC Med Res Methodol. 2008 Oct 9;8(1):65.

45. Instituto Nacional de Estadistica E Informatica. Estadisticas. Poblacion y Vivienda. Poblacion Ttoal al 30 de Junio, POr Grupos Quinquenales de Edad, Segun Departamento, Provincia y Distrito, 2015 [Internet]. 2015. Available from: https://www.inei.gob.pe/estadisticas/indice-tematico/poblacion-y-vivienda/

46. Instituto Naciona De Salud. Sistema de informacion del estado nutricional (SIEN). 2017 [Internet]. Available from: https://web.ins.gob.pe/es/alimentacion-y-nutricion/vigilancia-alimentaria-y-nutricional/vigilancia-del-sistema-de-informacion-del-estado-nutricional-en-%20EESS

47. Rubio-Codina M, Araujo MC, Attanasio O, Muñoz P, Grantham-McGregor S. Concurrent Validity and Feasibility of Short Tests Currently Used to Measure Early Childhood Development in Large Scale Studies. PLOS ONE. 2016 Aug 22;11(8):e0160962.

48. Kelsey J, Whittemore A, Evans A, Thompson D. Methods in Observational Epidemiology. Monographs in Epidemiology and Biostatistics. Second Edition. Vol. 26. New York: Oxford University Press; 1996.

49. Fernald LCH, Kariger P, Hidrobo M, Gertler PJ. Socioeconomic gradients in child development in very young children: evidence from India, Indonesia, Peru, and Senegal. Proc Natl Acad Sci U S A. 2012 Oct 16;109 Suppl 2:17273–80.

50. Fernald L, Kariger P, Engle P, Raikes A. Examining Early Child Development in Low-Income Countries: A Toolkit for the Assessment of Children in the First Five Years of Life. The World Bank; 2009.

51. Rubio-Codina M, Araujo MC, Attanasio O, Grantham-McGregor S. Validez concurrente y viabilidad de pruebas cortas comunmente usadas para medir el desarrollo infantil temprano en estudios a gran escala: Metodologia y resultados. Banco Interam Desarro [Internet]. 2016 Agosto;(723). Available from: https://publications.iadb.org/bitstream/handle/11319/7823/Validez-concurrente-y-viabilidad-de-pruebas-cortas-comunmente-usadas-para-medir-el-desarrollo-infantil-temprano-en-estudios-a-gran-escala-metodologia-y-resultados.pdf

52. Rubio-Codina M, Attanasio O, Grantham-McGregor S. Mediating pathways in the socio-economic gradient of child development: Evidence from children 6–42 months in Bogota. Int J Behav Dev. 2016 Nov 1;40(6):483–91.

53. McCoy DC, Waldman M, Fink G. Measuring early childhood development at a global scale: Evidence from the Caregiver-Reported Early Development Instruments. Early Child Res Q. 2018 Oct 1;45:58–68.

54. McCoy DC, Fink G, Pierre-Louis M. CREDI. Caregiver-Reported Early Development Instruments. User Guide. [Internet]. 2018. Available from: sites.sph.harvard.edu/credi/

55. Tran NT, Portela A, de Bernis L, Beek K. Developing Capacities of Community Health Workers in Sexual and Reproductive, Maternal, Newborn, Child, and Adolescent Health: A Mapping and Review of Training Resources. PLoS ONE [Internet]. 2014 Apr 15 [cited 2017 Jul 21];9(4). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3988080/

56. Crigler L, Hill K, Furth R, Bjerregaard D. Community Health Worker Assessment and Improvement Matrix (CHW AIM): A Toolkit for Improving Community Health Worker Programs and Services. Revised Version. Published by the USAID Health Care Improvement Project. Bethesda, MD: University Research Co., LLC (URC). 2013.

57. Basic Support for Institutionalizing Child Survival (BASICS) and the Prevention of Postpartum, Hemorrhage Initiative (POPPHI). Training Community Health Workers to Give Maternal and Newborn Health Messages: A Guide for Trainers. Arlington, Va., USA: for the United States Agency for International Development (USAID). 2009.

58. Perry H, Crigler L. Developing and Strengthening Community Health Worker Programs at Scale: a reference guide and case studies for program managers and policymakers. [Internet]. Maternal and Child Health Integrated Program; 2014. Available from: http://www.mchip.net/CHWReferenceGuide

59. Ministerio de Salud. Preparando al Agente COmunitario de Salud para el Cuidado Integral de la Salud y Nutricion de las Gestantes y de las Niñas y Niños Menores de 5 años - “El Manual del Agente Comunitario de Salud.” Ministerio de Salud del Peru; 2009.

60. Ministerio de Salud DG de P de la S. Orientaciones Para El Fortalecimiento de la Labor Del Agente Comunitario de Salud. Ministerio de Salud del Peru; 2014.

61. Organizacion Panamerican de la Salud. Manual del Agente Comunitario de Salud: Manual del Facilitador. Organizacion Mundial de la Salud; 2010.

62. Epi Info™ | CDC [Internet]. 2017 [cited 2018 Sep 13]. Available from: https://www.cdc.gov/epiinfo/index.html

63. ATLAS.ti: The Qualitative Data Analysis & Research Software [Internet]. [cited 2018 Sep 13]. Available from: https://atlasti.com/

16. FIGURE LEGENDS

Figure 1. Theory of Change

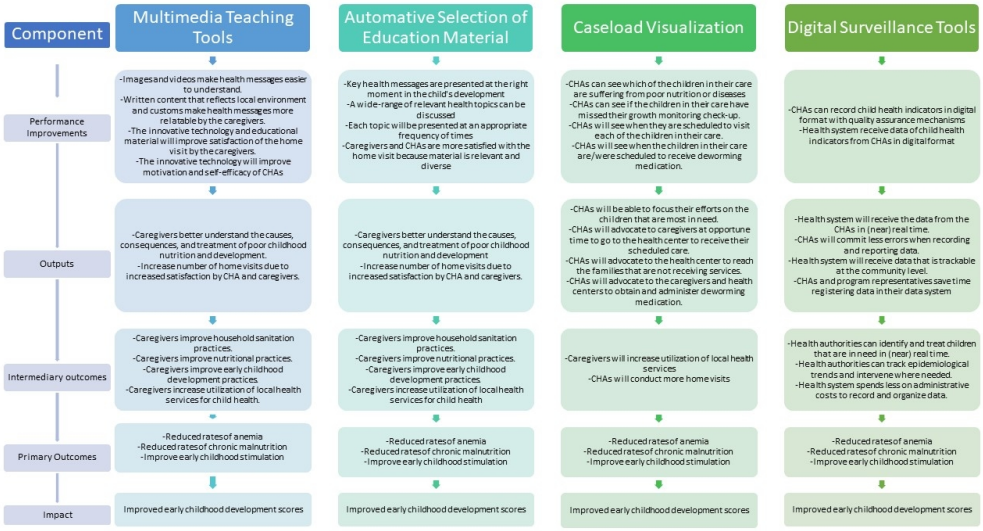


Figure 1

338x190mm (96 x 96 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	___2 and 11___
	2b	All items from the World Health Organization Trial Registration Data Set	__2 and 12____
Protocol version	3	Date and version identifier	__2_____
Funding	4	Sources and types of financial, material, and other support	__12_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	__12_____
	5b	Name and contact information for the trial sponsor	__12_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	__12_____
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	__12_____

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	__2-4_____
	6b	Explanation for choice of comparators	__10-11_____
Objectives	7	Specific objectives or hypotheses	___5_____
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	___5-7_____
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	__5-6_____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	___6_____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	___9-10_____
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	____NA_____
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	___10_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	___NA_____
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	____4-5_____
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	____12-13___

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	__6-7_____
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	___6_____
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	___5_____
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	__NS_____
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	___5_____
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	____NA_____
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	___NA_____
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	__7-11_____
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	____10-11_____

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	_____11___
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	____11_____
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	____NA_____
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	____NA_____
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	___11_____
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	___11_____
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	____NA_____
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	____NA_____
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	___11_____
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	___NA_____

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	___12_____
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	___NA_____
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	___12_____
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	___12_____
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	___12_____
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	___NA_____
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	___12_____
	31b	Authorship eligibility guidelines and any intended use of professional writers	___NA_____
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	___12_____
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	___NA_____
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	___NA_____

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

An mHealth Tool to Improve Community Health Agent Performance for Child Development: Study Protocol for a Cluster-Randomized Controlled Trial in Peru

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-028361.R2
Article Type:	Protocol
Date Submitted by the Author:	13-Sep-2019
Complete List of Authors:	Westgard, Christopher; University of North Carolina at Chapel Hill Gillings School of Global Public Health, Department of Maternal and Child Health; Elementos, Department of Research Rivadeneyra, Natalia; Elementos, Department of Research Mechael, Patricia; HealthEnabled
Primary Subject Heading:	Global health
Secondary Subject Heading:	Health services research, Research methods, Evidence based practice, Health informatics
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, early childhood develoment, Nutrition < TROPICAL MEDICINE, Community child health < PAEDIATRICS, community health worker, Implementation Science

An mHealth Tool to Improve Community Health Agent Performance for Child Development: Study Protocol for a Cluster-Randomized Controlled Trial in Peru

Christopher Westgard[1,2,*]
cmwestgard@unc.edu

Natalia Rivadeneyra[2]
rivadeneyra.natalia@gmail.com

Patricia Mechael[3]
patty@healthenabled.org

1. Department of Maternal and Child Health, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, North Carolina, USA
2. Department of Research, Elementos, Lima, Peru
3. HealthEnabled, Cape Town, South Africa

[*]Corresponding Author:
Jiron Domeyer 105, Barranco, Lima, Peru
cmwestgard@unc.edu
+51.927.980.400

Word Count: 5227

1. ABSTRACT

Introduction: Cultivating child health and development creates long-term impact on the well-being of the individual and society. The Amazon of Peru has high levels of many risk factors that are associated with poor child development. The use of 'community health agents' (CHAs) has been shown to be a potential solution to improve child development outcomes. Additionally, mobile information and communication technology (ICT) can potentially increase the performance and impact of CHAs. However, there is a knowledge gap in how mobile ICT can be deployed to improve child development in low resource settings.

Methods and Analysis: The current study will evaluate the impact of a tablet-based application that intends to improve the performance of CHAs during their home visits with children under 4. The App will guide the CHAs through the steps of an effective home visit and provide images and videos to teach key health messages. The App will organize their caseload and provide a mechanism to record child health indicators. The impact will be evaluated through an experimental cluster randomized controlled trial. The clusters will be assigned to the intervention or control group based on a covariate-constrained randomization method. The impact on child development scores, anemia, and chronic malnutrition will be assessed with an analysis of covariance (ANCOVA). The secondary outcomes include knowledge scores by caregivers of healthy child-rearing practices, self-efficacy, and use of health services. The study will be implemented in the Amazon region of Peru. The results of the study will provide evidence on the potential of a mHealth tool to improve child health and development indicators in the region.

Ethics and Dissemination: The protocol and instruments were approved by the Institutional Ethics Committee of the National Hospital "San Bartolome" on Nov. 8, 2018 (IRB Approval #15463-18). The trial is registered in the ISRCTN Registry at, ISRCTN43591826.

Keywords: mHealth, ICT, implementation science, impact evaluation, maternal and child health, early childhood development, anemia, malnutrition, community health workers, Peru, Amazon.

2. ARTICLE SUMMARY

2.1. Strengths and Limitations of This Study

- The intermediate variables will be assessed to measure the behavior changes that occurs along the theory of change. The study will be able to evaluate the various mediator variables that are expected to contribute to the final objective.
- A process evaluation with qualitative assessments will be used to identify issues of implementation and inform the implementation plan for scalability.
- The mHealth tool and the monitoring and evaluation strategy provides a surveillance mechanism that will allow for continuous feedback on the use of the intervention tool and health status of the study group.
- Child development will be assessed by a parent reported survey. Although the instrument has been shown to have high correlation to directly observed survey, there is more potential for parent created biased.
- The secondary outcomes that measure changes of the CHAs will be underpowered due to limitations in the sample size of CHAs.

3. BACKGROUND

In low and middle-low income countries millions of children under the age of 5 never reach their cognitive, linguistic and socio-emotional potential (1,2). Chronic malnutrition, anemia and iodine deficiency delay the physical and cognitive development of children, reduce their level of energy, and weaken their immune system. Child development can also be delayed by low levels of early

childhood stimulation (1,3). In the Peruvian Amazon there is a high prevalence of various risk factors associated with developmental delay, especially in rural areas. A study conducted in 2017 showed that the prevalence of developmental delay in the Amazon of Peru was 26.7% (4). In the Amazonian department of Loreto, the prevalence of childhood anemia is 49.9% and chronic malnutrition is 23.6% (2017) (5). Those indicators are worse in indigenous communities (6–9).

The well-being of children in communities can be greatly increased by improving families' understanding of healthy child-rearing practices. Health promotion strategies that establish an intercultural dialogue with families do a better job at promoting healthy practices (10,11). A program can train and support community members to conduct health promotion that can create behavior changes and improve child development outcomes. Community Health Agents (CHAs) can play an essential role in reducing inequalities in health services by acting as a link between communities and the local health services (11–13). The CHA can establish a warm relationship with the caregiver, thus increasing the acceptance of health advice, improving the absorption of knowledge and getting caregivers involved in the identification and resolution of their own health problems (14–21). The positive impact of CHAs has been associated with a reduction in malnutrition, anemia, malaria, cases of diarrhea, improved child development, and other health indicators (11,22,23). Therefore, understanding and improving the performance of CHAs can greatly improve behavioral outcomes of caregivers, increase the utilization of local health services, and enhance the overall health and well-being of communities (14,24–31).

Several studies have shown that a mobile information and communication technology (ICT) can improve the performance of CHAs in their ability to perform health promotion, collect and report timely information regarding family health, provide health services such as vaccines, and refer families to appropriate local health services (32–39). Additionally, when a mobile ICT tool is used by a CHA, the device can increase the confidence the caregivers have in the messages being transmitted and increase the confidence the CHAs have in their own work (32,33,37,38,40,41). Through implementation science, innovations in mobile ICTs and strategies for child health and development can be extended to low resource settings to empower local actors and spread the benefits of advancements in technology (35,36).

A study on the performance of CHAs in the Peruvian Amazon identified difficulties they face in their work. They had difficulty providing a clear explanation of the causes of common diseases, remembering essential steps of home visits, and diversifying the health topics that were discussed (29). As described above, an mHealth tool could help the CHAs overcome some of the difficulties they have in conducting an effective home visit. However, there is currently little evidence on the impact of an mHealth tool when used as an educational device by CHAs to improve child development (33). Additionally, there is a knowledge gap on the impact that an mHealth tool can have when utilized by CHAs in rural regions of Peru. Therefore, the present study aims to demonstrate the impact of an mHealth tool used for health promotion and surveillance by CHAs to improve child development in the Peruvian Amazon.

4. HYPOTHESIS

The study hypothesizes that an mHealth tool with digital educational content developed for the local context will improve the capacity of the CHAs to transmit health messages to the caretakers, thus creating behavior change that will lead to better health and child development outcomes for the children. The hypothesis is based on a theory of change that tracks the mediating variables and considers the potential outputs and outcomes that are expected occur as a result of the intervention (42). The theory of change displayed in Figure 1 highlights the various components that are included in the tablet-based application and unfolds the expected outcomes of each. The

theory of change is presented as a comparison to the status-quo; traditional CHA programs in Peru that use paper-based reporting and educational material.

Based on the Theory of Change, the study has the following hypotheses:

H1: The mHealth tool will improve the performance of CHAs during their home visits with children, as measured by doses, content, and inter-personal relationships.

H2: Improved performance by CHAs will increase knowledge acquisition and healthy child-rearing practices by caregivers.

H3: Improved knowledge and healthy practices by caregivers will improve the health and development of the children that receive the intervention.

5. OBJECTIVES

5.1. Main Aim

The objective of the study is to evaluate the impact of the mHealth tool (tablet with application) on child development and nutrition status of children aged 6 to 36 months compared to children who receive home visits from CHA without the mHealth tool.

5.2. Primary Outcomes

1. *[Primary Objective]* Improve child development scores for the children in the intervention group in the domains of language, cognition, gross motor, and social-emotional by 20% compared to the children in the control group ($p<0.05$).
2. Decrease the prevalence of anemia in children by 20% compared to the baseline measurement.
    a. Children in the intervention group will experience a greater reduction in the prevalence of anemia than children in the control group ($p <0.05$)
3. Decrease the prevalence of chronic malnutrition in children by 15%, compared to the baseline measurement.
    a. Children in the intervention group will experience a greater reduction in the prevalence of chronic malnutrition than children in the control group ($p <0.05$).

5.3. Secondary Outcomes

The secondary outcomes of the intervention include indicators of behavior change by CHA and families that have established causal connections with improved health and child development. The intervention is expected to achieve the following secondary outcomes:

4. The caregivers of the intervention group will improve knowledge evaluation scores by 50% compared to the baseline measurement.
5. CHAs in the intervention group will improve their performance evaluation scores by 50% compared to the baseline measurement.
6. More than 50% of the CHAs in the intervention group will express improved satisfaction and self-efficacy when compared to the baseline data.
7. The caregivers of the intervention group will use the local health services for children's health more frequently than they did during the baseline.

6. METHODS

6.1. Study Design

The impact will be evaluated through an experimental cluster randomized controlled trial. Each cluster represents a CHA because the children that receive visits from the same CHA must receive the same intervention. Each cluster will be matched with a second cluster using covariate-constrained randomization (43). Recruitment and baseline surveys will be conducted before allocation to the intervention or control group for each cluster. The variables that will be used to covariate-constrained randomization include: the size of the community, type of health facility in the community, and distance to the nearest health center (level I-2), and prevalence of anemia. For each cluster pair, one cluster will be randomly assigned to the intervention group and the other to the control group. The covariate-constrained randomization will be conducted with an open-sourced algorithm and the program, R (44).

6.2. Location

The study will be implemented in the Amazon region of Peru. The study will be carried out in the department of Loreto, province of Maynas, and districts of Mazan, Punchana, and Indiana. The district of Mazan has a population of 13,779 (45), a prevalence of chronic malnutrition of 24.4% and a prevalence of anemia at 39.1%, in 2017 (46). The capital of the district of Mazan is located approximately one and a half hours by boat from the capitol city of the province, Iquitos. The district of Punchana has a population of 91,128 (45), a prevalence of chronic malnutrition of 22.7% and a prevalence of anemia of 39.9% (46). The capital of Punchana, is 20 minutes from the city of Iquitos. The district of Indiana has a population of 11,301 (45), a prevalence of chronic malnutrition of 22.4%, and a prevalence of anemia at 46.7%, in 2017(46). The capital of the district to Indiana is 1.5 hours by boat from the city of Iquitos.

The research team with the support of the Regional Ministry of Health of Loreto, will choose the communities that will be included in the study after traveling to the communities to ensure they meet the selection criteria. The study communities must have the following characteristics:

- Has an active CHA that visits families in their community.
- Is not a participant in another health related study.
- Is located less than 6 hours from Iquitos.
- Has at least 25 families and a maximum of 1500 families.

The communities must have an active CHA program for the study to be because we are measuring the impact of included the mHealth tool in existing CHA programs. The community cannot be participating in another study that includes an intervention that was/will be implemented due to the confounding variables that would cause in our study and the other study. The communities must be less than 6 hours from Iquitos due to budgetary restraints that hinder the research team's ability to consistently travel 6 or more hours to execute the study. The size limitation of the community is required to ensure the study obtains a minimum number of children that are reached per tablet/CHA.

6.3. Participants and Sample Size

The study population includes:

- 10-14 communities, half in the intervention group and half in the control group.
- 40-50 CHAs, half CHAs in the intervention group and half CHAs in the control group.
- 400-450 children, half in the intervention group and one half in the control group

All children between 0 - 36 months in the communities will receive visits from a CHA, in the intervention and control group. However, only the CHAs in the intervention group will receive a tablet with the application to assist their home visits. All the children in the intervention group will have the opportunity to receive the intervention with the tablet.

To assess the impact of the intervention, a sample of the population will be chosen at random to receive the evaluation. The inclusion criteria for the study sample are the following:

- Children who belong to one of the communities included in the study, aged 6 to 36 months.
- Primary caregiver of the child is older than 15 years.
- The caregiver is willing to receive visits from the CHA.

The minimum age of children to be included in the impact evaluation is determined by the quality of the early childhood development tools. Assessment of child development is more accurate with children older than 5 months (47). The maximum age of the children for the study is determined by the CHA program, which limits home visits by CHAs to children up to 36 months old. The minimum age of the caregiver is 16 because that is the age determined by the communities and the local ethics committee to be capable of giving an informed consent. It is important to capture information from mothers below 18 years old because 39% of the mothers in the region have their first child before the age of 17 (4). Caregivers that do not want to receive visits from CHAs will be excluded because they will not receive the intervention, nor be included in the control group.

The exclusion criteria for the study sample are:

- Families where the main caregiver or the child does not speak Spanish.
- Families that do not want to receive home visits from CHAs.
- Children with mental or physical disabilities.

Families that do not speak Spanish cannot be included because the study does not have appropriate translators for indigenous languages. Children with disabilities will be excluded in the evaluation because the child development evaluation tool is not equipped to evaluate children with these conditions. However, children with disabilities will still receive the intervention.

The sample size for the evaluation is calculated to measure the effect size on the primary outcome indicator, child development. A study in the Amazon region of Peru (2017) determined that the standard deviation of communication scores, determined by the Ages and Stages Questionnaire, was 15.19 (4). The current study predicts a 20% increase in child development scores, which will result in an effect size of 0.49 (average communication score was 37.48, a 20% increase is 44.98, 0.49 standard deviations) (data available in public repository) (4). To calculate the minimal sample size needed, the following parameters were determined:

- Two-sided significance level: 0.05
- Power: 90%
- Effect Size: 0.49
- Avg. Cluster Size: 9
- Intra Cluster Correlation (ICC): 0.15
- Variance Inflation Factor (VIF): 2.2

The following calculation is used to determine the sample size:

$$N \text{ per group} = \frac{[(z_{alpha} + z_{beta})^2 \times 2 \times SD^2]}{\text{Expt'd diff}^2} = \frac{(1.96 + 1.28)^2 \times 2 \times 15.19^2}{(15.19 \times .49)^2}$$

The sample size per group (t-test) with no clusters would be 88. To control for the Intra-Cluster Correlation (ICC), the per group sample size (88) is multiplied by the Variance Inflation Factor (VIF=1+(Avg. Cluster Size–1)*ICC=2.2) to determine the minimal sample size to be **193 per group** (48). The study will include 21 clusters and 9 children and caregivers per cluster.

55.34

6.4. **Instruments**

To measure the impact of the intervention and understand the perspective of the users, a series of instruments will be applied to the study participants. The instruments include; evaluation of child development, attitudes and practices questionnaire, knowledge evaluation, performance evaluation of CHAs, and collection of anemia and anthropometric indicators. Qualitative surveys will also be used to evaluate the satisfaction of CHAs and caregivers in relation to the intervention.

The questionnaires and evaluations will be carried out in the homes of the participants. The researcher will ask if a caregiver of a child within the age range is in the home, if so they will explain the study and ask the caregiver if they want to participant and are willing to sign the informed consent. The researcher will record the responses of the questionnaires and evaluation on a smart phone or electronic tablet.

6.4.1. Evaluation of Child Development

Child development can be effectively evaluated with an instrument that utilizes caregiver-reported data to assess the ability of the child to perform age-relevant developmental activities (47,49–52). The current study will use the Caregiver-Reported Early Development Instrument (CREDI) to evaluate child development (53,54). The CREDI has been validated as an effective instrument to evaluate child development, including low-resource settings in 17 countries (54). The CREDI is effective for large-scale, population-wide studies because it requires less time, materials, and evaluator expertise than other similar instruments (53).

The CREDI is conducted by asking the caregiver if the child is currently capable of completing a list of age-appropriate activities, in which the caregiver can respond by indicating; yes, no, or I don't know. The CREDI will provide a developmental score and a classification that represents the child's development trajectory as; normal development or at risk of developmental delay. These classifications will be used as the primary dependent variables of the study.

6.4.2. Attitudes and Practices Questionnaire

The study will use a quantitative questionnaire to measure the attitudes and practices of caregivers that influence maternal and child health. The following topics are included in the questionnaire: demographic information, safe pregnancy practices, feeding practices, prevention of illnesses, early childhood stimulation, and use of local health services. The questionnaire will be conducted with all caregivers of the children included in the study. The questionnaire will take approximately 10 minutes.

6.4.3. Knowledge Evaluation

To assess the knowledge of caregivers of healthy practices for maternal and child health, an instrument was built based on the literature (13,55–57). The Knowledge Evaluation asks the caregiver questions regarding maternal and child health, nutrition, sanitation, and infectious diseases. The questions are open-ended to give the caregiver the opportunity to provide multiple answers that displays their knowledge of the topic.

The Knowledge Evaluation will take place directly after the Attitudes and Practices Questionnaire. The Knowledge Evaluation will be scored by giving the participant 1 point for every correct answer they provide. The correct answers will be added together to provide a total "Knowledge Score" for the caregiver.

6.4.4. Performance Evaluation of CHAs

The Performance Evaluation of CHAs was based on an instrument built by the University of West Indies and the Inter-American Development Bank to measure the quality of home visits by CHAs (14). The Performance Evaluation includes questions related to the use of materials, activities, promotion of child development, relationship between CHA and caregivers, and relationships between the CHA and the child. The Performance Evaluation was modified and validated during a previous study in the Amazon region within the local CHA program. The instrument provides further focus on health messages provided by the CHA and the needs of the communities in the Amazon (29).

The conduct the performance evaluation, the researcher will accompany the CHA on their home visit with a child to observe the home visit. The researcher will observe the home visit in silence, trying not to influence the dynamic of the visit. The researcher will take notes during the visit and complete the Performance Evaluation immediately after the conclusion of the home visit.

*6.4.5.*Survey of the Use of Local Health Services

The research team will survey the local health centers in the communities to obtain statistics regarding the use of health services related to maternal and child health, including: child growth monitoring check-ups, prenatal check-ups, immunization coverage, distribution of micronutrient supplements, distribution of anti-parasitic medicine, and distribution of oral rehydration salts for diarrhea. The survey will be conducted with the nurse that conducts maternal and child health evaluations at the health center. The survey will take approximately 15 minutes and can be filled out independently by the health post representative.

*6.4.6.*Survey of Child Health Indicators

The CHEST application will be used to collect child health indicators by CHAs during their home visits. The children have a card with information that was recorded during their growth monitoring check-ups at the local health center, including height, weight, age, vaccines, and hemoglobin levels (when tested). The CHA will observe the information written on the card and record it with the CHEST application. The CHA will also ask additional questions regarding the health of the child, including incidences of diarrhea, cough, fever, malaria and other illness. The data from the application will be uploaded to the secured server when the CHA or supervisor has access to the cellular network.

*6.4.7.*Questionnaire on Satisfaction and Self-Efficacy of CHAs

The Questionnaire on Satisfaction and Self-Efficacy of CHAs will be used to measure the degree satisfaction and self-efficacy the CHAs have from using the CHEST application during their home visits. The questions are both quantitative and qualitative. The CHAs will have the opportunity to describe how the experience with the tablet could be improved.

*6.4.8.*Questionnaire on Satisfaction of Caregiver

The Questionnaire on Satisfaction of caregivers will be used to measure the degree satisfaction of the caregivers that received the intervention. The questions are both quantitative and qualitative. The caregivers will have the opportunity to describe what they like and don't like about the use of a tablet during the home visits.

6.5. **Patient and Public Involvement**

The study was created through formative research done in the same communities to identify their needs and desires related to improving child health and development. A performance evaluation study was conducted with the CHAs in the region by the author (29). In the study, the CHAs and caregivers expressed their need and desire for more information regarding topics of health and child development. The current intervention was created to address those needs.

The results of the study will be presented to the participants, including the community health agents, caregivers, health facility personal, and Regional Ministry of Health in the form of a study brief that indicates the results of each indicator collected. The results will be presented to the public via publication of results in an international scientific journal.

Patients were not involved in the design or recruitment of the study.

7. INTERVENTION

The intervention includes the development and implementation of a tablet-based application (CHEST) to improve the performance of the CHAs during their home visits. The CHAs will use the CHEST Application during their home visits to teach caregivers good health practices and early childhood stimulation. The application will provide the steps for the CHA to follow to conduct an effective home visit. The application will include videos and images to show the caregiver to transmit key health messages. Also, the application will organize the case load of children of the CHA and will provide a mechanism to record maternal and child health indicators.

The intervention is described in the following five phases:

7.1. **Phase 1: Preparation of Material**

7.1.1. Step-by-Step Agendas for Home Visits

The research team will work with the Regional Ministry of Health of Loreto to build agendas for home visits by the CHAs. The health messages for the home visits are based on national and international manuals for home visits by CHAs to teach maternal and child health and development (58–61). The agendas include steps to follow by the CHA to provide a quality home visit and collect child health indicators. The messages included in the agendas include; what nutritious foods should be consumed by children, how to avoid diarrhea and other diseases, good practices of early attention, and use of health services. There will be 1 agenda for each month of age of the child (1-36 months).

7.1.2. Multimedia Material

The research team will generate multimedia material to be used in the application to transmit health messages. The content will be designed to convey the health messages clearly within the local culture in the Amazon. The material will include videos of people from the region acting out health topics, instructional videos on early childhood stimulation, and animations that describes health issues. In addition, the application will include educational images that have been developed by the regional Ministry of Health of Loreto and other institutions.

7.2. **Phase 2: Development of the Application**

The research team will evaluate the mHealth applications that have been developed and are open source to determine which will be best to adapt for the current project. The project will contract a team of program developers to modify the open source application to fit the current objectives and

local context. The program developer will include the agendas, multimedia, and data collection mechanisms in the application. The application will function without internet signal and protect all information by password.

7.3. **Phase 3: Baseline Data Collection**

The research team will conduct the surveys and evaluations in the intervention and control communities to obtain a baseline for the study. The instruments that will be applied for the baseline survey include the *Child Development Evaluation, Attitudes and Practices Questionnaire, Knowledge Evaluation, Performance Evaluation of CHA, and Survey on the Use of Health Services*. The baseline survey will be completed before implementation beings in the intervention and control communities.

7.4. **Phase 4: Implementation of Intervention**

7.4.1. Training Workshops

The research team will conduct training workshops with the CHAs in the intervention group to teach them how to use the tablet and application. The workshops will occur during a period of 3 days, 4 hours per day. The leaders of the health facility and Regional Ministry of Health of Loreto will be invited to participate in the workshops and in the supervision of the development of the project.

7.4.2. Distribution of Tablets

After the training workshops, the research team will give a tablet to each CHA in the intervention communities. The CHAs will be instructed to bring the tablet to local health center if they are having problems with the tablet or to store the tablet in their home until a member of the monitoring team visits their community. A supervisor of the CHA program will visit the CHAs to ensure the App is being used and functioning correctly.

7.4.3. The Intervention

The CHAs will continue to conduct home visits with the children in their caseload the same as before the distribution of the tablets. The only change is that the CHAs will use the tablets during the home visits. The number of home visits depends on the demands placed by the community and the motivation of the individual CHA. The CHAs in the communities typically conduct 1-4 home visits per month with children aged 0-36 months. The CHAs are instructed to teach the caregivers good sanitation, nutrition, and child development practices.

The CHAs will use the tablet-based app to visualize the health indicators of the children in their caseload, record health indicators of the child during each visit, observe and chare images and videos that will help teach health and development messaging, and send data to a central database. The App will guide the CHA through each step of the home visit. The supervisor of the CHA program will visit the CHAs to ensure they can upload their data to the database. This include, in some cases, carrying the tablet to a community that has signal to upload the data.

7.4.4. Monitoring

The research team will supervise the work of the CHAs through observations of their home visits and interviews with families and CHAs in the communities. The research team will visit the communities every month during the first 4 months, and less frequently when they see that the program is working as it should.

The team will also track activities of the CHAs through the data uploaded by the application. They will be able to track the number of visits being conducted and the health indicators of the children.

If the tablet is not uploading data to the survey, the research team will visit the community to identify the problem.

The local health facility will also have access to the data and will be able to identify if a child is at risk of chronic malnutrition, chronic diarrhea and/or is not attending growth monitoring check-ups.

7.5. **Phase 5: Evaluation of the Intervention**

At the end of the intervention, the follow-up survey will be carried out in the intervention and control communities. The instruments included in the follow-up survey include the *Evaluation of Child Development, Attitudes and Practices Questionnaire, Knowledge Test, Performance Evaluation of CHA, Survey of Use of Health Services, Questionnaire on Satisfaction and Self-Efficacy of CHA*, and *Questionnaire on Satisfaction of Caregivers*.

The data gathered by the application will be used to evaluate the child heath indicators and the number of home visits conducted.

8. DATA ANALYSIS

The quantitative data obtained in the surveys will be organized and analyzed with the statistical software, Epi Info version 7.1.4.0 (62). The qualitative data will be organized and analyzed with the program Atlas.ti (63). To carry out the impact analysis, four mathematical models will be used to interpret the results, generating an optimal analysis to understand the interactions between the variables. The analysis will be conducted on the dependent variable to test the primary outcome, as well as the intermediary variables to test the secondary outcomes and measure the mediating effect of those variables. First, a descriptive analysis will be performed to compare indicators between the analysis groups, including average and frequencies of the independent and dependent variables. Second, a bivariate analysis with Chi-square test will be done to examine the associations between the independent and the dependent variables. Third, a multivariate regression analysis will be used to examine the interactions between the independent variables and the dependent variables. Fourth, an analysis of covariance (ANCOVA) regression method will be used to calculate the impact of the intervention (43).

8.1. **Data Monitoring**

Data monitoring will be completed by the Data Monitoring Committee to ensure non-biased handling and analysis of data obtained from baseline, monitoring, and follow-survey. The Data Monitoring Committee will be made up of the team of experts that will be hired to create the content of the intervention and mentors that guided the research team. The Data Monitoring Committee will each guard files of data at different time points so they can later be crossed reference to ensure consistency. The Data Monitoring Committee will not include permanent members of the sponsor organization or associates of the funding organization or anyone with competing interest or incentive for the intervention to be successful.

8.1. **Data security**

All data will be stored in a secure encrypted server that is protected by password. All identifiable information in the data set will be deleted to make it impossible to link the data with the individual. Information regarding contact information of CHAs will be stored on the secure server. There will be no need to maintain identifies within the data because there will be no follow-up serves with individuals. Members of the Data Monitoring Committee will ensure all identifiable information has been removed from the data set.

9. ETHICAL CONSIDERATIONS

The investigation was approved by the Ethics Committee of the National Hospital "San Bartolomé" on November 8, 2018 (Exp. Number 15463-18, Oficio N. 0744-2018-OADI-HONADOMANI-SB)

The investigation will include only those individuals that are willing and able to give their consent to be included in the study. The participant must be able to understand the information presented to them and voluntarily express their choice of whether they want to participate or not. The caregivers must be over 15 years of age to participate in the study.

It will be clearly stated that participation in the study will not compromise the health of the participants or violate any rights of the child. There will be no financial compensation for participation in the study. No biological samples will be collected, nor any medical or pharmacological treatments delivered in the research process. There are no possible adverse effects associated with participation in the study. There is the possibility of generating discomfort in the participants because the visits and surveys imply an investment of time. Given this, participants will be informed about the amount of time involved for their participation in the survey before signing the informed consent.

After completion of the child development evaluation the results will be immediately shared with the caretaker along with recommendations of early childhood stimulation activities that could benefit the child. Likewise, the results of the evaluations will be communicated to the health center of the community with a copy of a list of the children who are at risk of developmental delay. The child development evaluation represents a direct benefit to the participants in the intervention and control group.

The research team will monitor the intervention for at least 12 months to ensure the CHAs receive support, and the tablets receive maintenance or are replaced if need. The CHAs can opt-out of the intervention at any time, thus returning to their traditional methods of reporting and health promotion. After 12 months, the program will be handed over to the Municipality and they will continue to receive support as needed. The Municipality has been active in the design of the material for the intervention and will be active in the monitoring and evaluation efforts. The Municipality members will be trained in how to manage and sustain the program.

The results obtained from the study will be made publicly accessible through the publication of finding and a report delivered to the local health authorities. The dataset will available in a public data repository.

9.1. Informed consent for caregivers

The Informed Consent for Caregivers includes the description of the study, the participation of the caregiver, the participation of the child, and the amount of time required to complete the survey. The interviewer that conducts the questionnaires will ask for consent from the caregiver. If the caregiver agrees to participate in the study, they will be asked to sign the Informed Consent form. The caregiver will be provided a copy of the consent.

9.2. Informed consent for CHA

The Informed Consent for CHAs includes a description of the study and the performance evaluation that will be conducted with the CHA. The interviewer that conducts the questionnaires will ask for consent from the CHA. If the CHA agrees to participate in the study, they will be asked to sign the Informed Consent for CHAs. The CHA will be offered a copy of the consent.

9.1. Consent to Publish

There will be no identifying images, personal details, or clinical details of participants presented that will compromise the anonymity of the participants in the study.

10.CONCLUSIONS

The results of the study will provide evidence on the potential of a mHealth tool to improve child health and development indicators in the region. The process evaluation with qualitative assessments will also be conducted to identify barriers, strengths, and weaknesses of the program.

11.ABBREVIATIONS

CHA – community health agents
CHEST – Child Health Education and Surveillance Tool
CREDI – Caregiver-Reported Early Development Instrument
ICT – Information and communication technology

12. DECLARATIONS

12.1. Availability of data and materials

The datasets generated during and analyzed during the current study will be stored in the publicly available repository, figshare (https://figshare.com/). De-identified participant data, including child development evaluation scores, anemia results, chronic malnutrition results, KAP survey results, and CHA performance evaluations, will be stored in the repository. The data will be available through the repository for 10 years. Data from participants will only be made available if consent was provided by the participant through the informed consent process.

12.2. Competing interests

The authors and members of the research team have no competing interest.

12.3. Communication of Trial Results

The results of the study will be presented to the participants, including the community health agents, caregivers, health facility personal, and Regional Ministry of Health in the form of a study brief that indicates the results of each indicator collected. The study brief will be written and described in a manner that is intelligible for the target population. The CHAs will be asked to distribute the brief and describe the findings to the individual families in their caseload.

The results will be presented to the public via publication of results in an international scientific journal. The research team will also seek opportunities to present the results in national and international conferences to disseminate findings.

12.4. FUNDING

The study is funded by the grant, Saving Brains, by Grand Challenges, Canada. The funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

12.5. AUTHOR CONTRIBUTIONS

CW conceived of the study. CW and NR contributed to the writing and revision of the protocol. PM provided advisory on study design. All authors contributed to refinement of the study protocol and approved the final manuscript.

12.6. **ACKNOWEDGEMENTS**

Special thanks to Liz Franco, Luis Orrego Ferreyros, Milagros Alvarado Llatance, and Gabriela Palacios Rojo for their assistance in developing the material and instruments of the study. Thanks to the Ministry of Development and Social Inclusion of Peru for their collaboration in designing the tool and identifying the participants and recipients of the study. Special thanks to Grand Challenges Canada for providing advisory service regarding study design, implementation strategies, and strategies to scale the intervention.

13.CHRONOLOGY

The study will last 24 months, beginning in October 2018 and ending in September 2020. The schedule of activities can be found in Table 1.

Table 1: Schedule of Activities

Activity	Oct	Nov	Dec	Jan '19	Feb	Mar	Apr	May	June	July-August	Sep-Dec	Jan-April '20	May-Aug '20
Complete Ethics Committee Protocol	■	■	■										
Develop home visit agendas			■	■	■	■	■	■					
Validate home visit material						■	■	■	■				
Create videos					■	■	■	■					
Develop Application		■	■	■	■	■	■	■					
Validate Application							■	■	■				
Recruit participants								■	■				
Baseline Survey								■	■				
Train CHAs									■				
Deploy App									■	■	■	■	■
Monitoring									■	■	■	■	■
Final Evaluation													■
End of Project													■

13.1. Flow Diagram schedule of activities

The Flow Diagram in Table 2 describes when intervention allocation and assessments of the study population will take place, in relation to the study activities.

Table 2: Flow Diagram

	Study Period				
	Enrolment	**Allocation**	***Post-Allocation***		***Close-out***
TIMEPOINT	$-t_1$	**0**	t_1	t_2	t_x
ENROLMENT:					
Eligibility screen of inclusion and exclusion criteria	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
Distribution of Tablet			♦—	—	—♦
Control group			♦—	—	—♦

ASSESSMENTS:					
Child development evaluation	X				X
Performance Evaluation	X				X
Knowledge, Attitudes, and Practices Survey	X				X
Monitoring of Community Health Agents		X	X	X	

14.TRIAL SPONSOR

Trial Sponsor: Elementos
Contact Name: Christopher Westgard
Address: Jiron Domeyer, Barranco, Lima, Peru
Telephone: +51927980400
Email: cmwestgard@unc.edu

15. REFERENCES

1. Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B. Developmental potential in the first 5 years for children in developing countries. The Lancet. 2007 Jan 6;369(9555):60–70.

2. Engle PL, Black MM, Behrman JR, Mello MC de, Gertler PJ, Kapiriri L, et al. Strategies to avoid the loss of developmental potential in more than 200 million children in the developing world. The Lancet. 2007 Jan 20;369(9557):229–42.

3. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. Lancet Lond Engl. 2011 Oct 8;378(9799):1325–38.

4. Westgard C, Alnasser Y. Developmental delay in the Amazon: The social determinants and prevalence among rural communities in Peru. PloS One. 2017;12(10):e0186263.

5. Instituto Nacional de Estadistica e Informatica. Loreto Compendio Estadistico 2017. Sistema Estadistico Nacional; 2017.

6. Anticona C, San Sebastian M. Anemia and malnutrition in indigenous children and adolescents of the Peruvian Amazon in a context of lead exposure: a cross-sectional study. Glob Health Action. 2014;7:22888.

7. Díaz A, Arana A, Vargas-Machuca R, Antiporta D. Situación de salud y nutrición de niños indígenas y niños no indígenas de la Amazonia peruana. US11 [Internet]. 2015 [cited 2017 Jan 26]; Available from: http://iris.paho.org/xmlui/handle/123456789/10008

8. Flores-Bendezu J, Calderon J, Rojas B, Alarcon-Matutti E, Gutierrez C. Chronic malnutrition and anemia in children under 5 years of indigenous households of Peru - Analysis of Demographic and Health Survey 2013. Fac Med 2015762135-40 Dxdoiorg1015381analesv76i211139.

9. Grantham-McGregor SM, Fernald LCH, Kagawa RMC, Walker S. Effects of integrated child development and nutrition interventions on child development and nutritional status. Ann N Y Acad Sci. 2014 Jan;1308:11–32.

10. Perry HB, Sacks E, Schleiff M, Kumapley R, Gupta S, Rassekh BM, et al. Comprehensive review of the evidence regarding the effectiveness of community–based primary health care in improving maternal, neonatal and child health: 6. strategies used by effective projects. J Glob Health [Internet]. [cited 2017 Nov 9];7(1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5491945/

11. Gilmore B, McAuliffe E. Effectiveness of community health workers delivering preventive interventions for maternal and child health in low- and middle-income countries: a systematic review. BMC Public Health. 2013 Sep 13;13:847.

12. Global Health Workforce Alliance, World Health Organization. Global experience of community health workers for delivery of health related millennium development goals: a systematic review, country case studies, and recommendations for integration into national health systems. 2010.

13. The Earth Institute. Millennium Villages Project. Community Health Worker Trainer's Manual. A guide to Home Based Services [Internet]. Version 2.1. Columbia University; 2013. Available from: http://millenniumvillages.org/wp-content/uploads/2014/09/CHWTrainingManual.pdf

14. Leer J, Lopez-Boo F, Perez Exposito A, Powell C. A Snapshot on the Quality of Seven Home Visit Parenting Programs in Latin America and the Caribbean. Inter-American Development Bank; 2016.

15. Schodt S, Parr J, Maria CA, Rubio-Codina M. La medición de la calidad de os servicios de visitas domiciliarias . Una revisión de la literatura. Danco Interamericano de Desarrollo; 2015.

16. Vogel CA, Caronongan P, Thomas J, Bandel E, Xue Y, Henke J, et al. Toddlers in Early Head Start: A Portrait of 2-Year-Olds, Their Families, and the Programs Serving Them. Volume 1: Age 2 Report. OPRE Report 2015-10 [Internet]. Administration for Children & Families; 2015 [cited 2017 Aug 3]. Available from: https://eric.ed.gov/?id=ED558558

17. Roggman LA, Cook GA, Innocenti MS, Jump Norman V, Boyce LK, Christiansen K, et al. Home Visit Quality Variations in Two Early Head Start Programs in Relation to Parenting and Child Vocabulary Outcomes. Infant Ment Health J. 2016 May 1;37(3):193–207.

18. Medina A, Sofía I. Evaluation protocol application of tasks for the socio - cognitive development in children from 37 to 71 months in the Program of Comprehensive Attention to Early Childhood Modality Family Environment District Secretariat of Social Integration [Internet]. [cited 2017 Aug 3]. Available from: https://intellectum.unisabana.edu.co/handle/10818/23587

19. Fernández S, Yonah R. Aplicación de ensayos domiciliarios para evaluar la adopción de prácticas mejoradas de alimentación complementaria en madres. Centro materno infantil Juan Pablo II. Villa El Salvador, Lima. 2005. Univ Nac Mayor San Marcos [Internet]. 2007 [cited 2017 Aug 4]; Available from: http://cybertesis.unmsm.edu.pe/handle/cybertesis/1121

20. Walker SP, Powell C, Chang SM, Baker-Henningham H, Grantham-McGregor S, Vera-Hernandez M, et al. Estrategias de apoyo parental a través de los servicios de salud en el Caribe [Internet]. BID; 2016 Feb [cited 2017 Aug 3]. Available from: http://repositorio.minedu.gob.pe/handle/123456789/4112

21. Chang-Say Chong A. La comunicación en los proyectos de lucha contra la desnutrición crónica infantil : el caso Ally Micuy (Áncash). Pontif Univ Católica Perú [Internet]. 2014 Sep 25 [cited 2017 Aug 3]; Available from: http://tesis.pucp.edu.pe/repositorio/handle/123456789/5598

22. Lewin S, Munabi-Babigumira S, Glenton C, Daniels K, Bosch-Capblanch X, Wyk BE van, et al. Lay health workers in primary and community health care for maternal and child health and the management of infectious diseases. Cochrane Database Syst Rev [Internet]. 2010 [cited 2018 Sep 19];(3). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004015.pub3/abstract

23. Lassi ZS, Kumar R, Bhutta ZA. Community-Based Care to Improve Maternal, Newborn, and Child Health. In: Black RE, Laxminarayan R, Temmerman M, Walker N, editors. Reproductive, Maternal, Newborn, and Child Health: Disease Control Priorities, Third Edition (Volume 2) [Internet]. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2016 [cited 2016 Jun 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK361898/

24. Howard KS, Brooks-Gunn J. The role of home-visiting programs in preventing child abuse and neglect. Future Child. 2009;19(2):119–46.

25. Singh V, Ahmed S, Dreyfuss ML, Kiran U, Chaudhery DN, Srivastava VK, et al. Non-governmental organization facilitation of a community-based nutrition and health program: Effect on program exposure and associated infant feeding practices in rural India. PloS One. 2017;12(9):e0183316.

26. Swider SM. Outcome Effectiveness of Community Health Workers: An Integrative Literature Review. Public Health Nurs. 2002 Jan 1;19(1):11–20.

27. Agarwal S, Perry HB, Long L-A, Labrique AB. Evidence on feasibility and effective use of mHealth strategies by frontline health workers in developing countries: systematic review. Trop Med Int Health TM IH. 2015 Aug;20(8):1003–14.

28. Mobile Healthcare Information for All. Assessment of mHealth applicaitons for their potential to provide essential healthcare information for citizens in low resource settings. HIFA; 2017.

29. Westgard C, Naraine R, Paucar Villacorta DM. Performance Evaluation of Community Health Workers: Case Study in the Amazon of Peru. J Community Health. 2018 Mar 26;

30. Ballard M, Montgomery P. Systematic review of interventions for improving the performance of community health workers in low-income and middle-income countries. BMJ Open. 2017 Oct 1;7(10):e014216.

31. Cometto G, Ford N, Pfaffman-Zambruni J, Akl EA, Lehmann U, McPake B, et al. Health policy and system support to optimise community health worker programmes: an abridged WHO guideline. Lancet Glob Health. 2018 Dec 1;6(12):e1397–404.

32. Ilozumba O, Dieleman M, Kraamwinkel N, Belle SV, Chaudoury M, Broerse JEW. "I am not telling. The mobile is telling": Factors influencing the outcomes of a community health worker mHealth intervention in India. PLOS ONE. 2018 Mar 27;13(3):e0194927.

33. van Heerden A, Sen D, Desmond C, Louw J, Richter L. App-Supported Promotion of Child Growth and Development by Community Health Workers in Kenya: Feasibility and Acceptability Study. JMIR MHealth UHealth [Internet]. 2017 Dec 5 [cited 2018 Sep 19];5(12). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5736876/

34. Lee S, Chib A, Kim J-N. Midwives' Cell Phone Use and Health Knowledge in Rural Communities. J Health Commun. 2011 Oct 1;16(9):1006–23.

35. Peterson HB, Haidar J, Fixsen D, Ramaswamy R, Weiner BJ, Leatherman S. Implementing Innovations in Global Women's, Children's, and Adolescents' Health: Realizing the Potential for Implementation Science. Obstet Gynecol. 2018 Mar;131(3):423–30.

36. Peterson HB, Haidar J, Merialdi M, Say L, Gülmezoglu AM, Fajans PJ, et al. Preventing maternal and newborn deaths globally: using innovation and science to address challenges in implementing life-saving interventions. Obstet Gynecol. 2012 Sep;120(3):636–42.

37. Källander K, Tibenderana JK, Akpogheneta OJ, Strachan DL, Hill Z, Asbroek AHA ten, et al. Mobile Health (mHealth) Approaches and Lessons for Increased Performance and Retention of Community Health Workers in Low- and Middle-Income Countries: A Review. J Med Internet Res. 2013;15(1):e17.

38. Prinja S, Nimesh R, Gupta A, Bahuguna P, Gupta M, Thakur JS. Impact of m-health application used by community health volunteers on improving utilisation of maternal, new-born and child health care services in a rural area of Uttar Pradesh, India. Trop Med Int Health TM IH. 2017;22(7):895–907.

39. Ilozumba O, Van Belle S, Dieleman M, Liem L, Choudhury M, Broerse JEW. The Effect of a Community Health Worker Utilized Mobile Health Application on Maternal Health Knowledge and Behavior: A Quasi-Experimental Study. Front Public Health [Internet]. 2018 May 7 [cited 2019 Apr 30];6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5949315/

40. Chib A. The Aceh Besar midwives with mobile phones project: Design and evaluation perspectives using the information and communication technologies for healthcare development model. J Comput-Mediat Commun. 2010 Apr 1;15(3):500–25.

41. Limaye NP, Rivas-Nieto AC, Carcamo CP, Blas MM. Nuestras Historias- Designing a novel digital story intervention through participatory methods to improve maternal and child health in the Peruvian Amazon. PLOS ONE. 2018 Nov 5;13(11):e0205673.

42. Lafferty CK, Mahoney CA. A Framework for Evaluating Comprehensive Community Initiatives. Health Promot Pract. 2003 Jan 1;4(1):31–44.

43. Ivers NM, Halperin IJ, Barnsley J, Grimshaw JM, Shah BR, Tu K, et al. Allocation techniques for balance at baseline in cluster randomized trials: a methodological review. Trials. 2012 Aug 1;13(1):120.

44. Carter BR, Hood K. Balance algorithm for cluster randomized trials. BMC Med Res Methodol. 2008 Oct 9;8(1):65.

45. Instituto Nacional de Estadistica E Informatica. Estadisticas. Poblacion y Vivienda. Poblacion Ttoal al 30 de Junio, POr Grupos Quinquenales de Edad, Segun Departamento, Provincia y Distrito, 2015 [Internet]. 2015. Available from: https://www.inei.gob.pe/estadisticas/indice-tematico/poblacion-y-vivienda/

46. Instituto Naciona De Salud. Sistema de informacion del estado nutricional (SIEN). 2017 [Internet]. Available from: https://web.ins.gob.pe/es/alimentacion-y-nutricion/vigilancia-alimentaria-y-nutricional/vigilancia-del-sistema-de-informacion-del-estado-nutricional-en-%20EESS

47. Rubio-Codina M, Araujo MC, Attanasio O, Muñoz P, Grantham-McGregor S. Concurrent Validity and Feasibility of Short Tests Currently Used to Measure Early Childhood Development in Large Scale Studies. PLOS ONE. 2016 Aug 22;11(8):e0160962.

48. Kelsey J, Whittemore A, Evans A, Thompson D. Methods in Observational Epidemiology. Monographs in Epidemiology and Biostatistics. Second Edition. Vol. 26. New York: Oxford University Press; 1996.

49. Fernald LCH, Kariger P, Hidrobo M, Gertler PJ. Socioeconomic gradients in child development in very young children: evidence from India, Indonesia, Peru, and Senegal. Proc Natl Acad Sci U S A. 2012 Oct 16;109 Suppl 2:17273–80.

50. Fernald L, Kariger P, Engle P, Raikes A. Examining Early Child Development in Low-Income Countries: A Toolkit for the Assessment of Children in the First Five Years of Life. The World Bank; 2009.

51. Rubio-Codina M, Araujo MC, Attanasio O, Grantham-McGregor S. Validez concurrente y viabilidad de pruebas cortas comunmente usadas para medir el desarrollo infantil temprano en estudios a gran escala: Metodologia y resultados. Banco Interam Desarro [Internet]. 2016 Agosto;(723). Available from: https://publications.iadb.org/bitstream/handle/11319/7823/Validez-concurrente-y-viabilidad-de-pruebas-cortas-comunmente-usadas-para-medir-el-desarrollo-infantil-temprano-en-estudios-a-gran-escala-metodologia-y-resultados.pdf

52. Rubio-Codina M, Attanasio O, Grantham-McGregor S. Mediating pathways in the socio-economic gradient of child development: Evidence from children 6–42 months in Bogota. Int J Behav Dev. 2016 Nov 1;40(6):483–91.

53. McCoy DC, Waldman M, Fink G. Measuring early childhood development at a global scale: Evidence from the Caregiver-Reported Early Development Instruments. Early Child Res Q. 2018 Oct 1;45:58–68.

54. McCoy DC, Fink G, Pierre-Louis M. CREDI. Caregiver-Reported Early Development Instruments. User Guide. [Internet]. 2018. Available from: sites.sph.harvard.edu/credi/

55. Tran NT, Portela A, de Bernis L, Beek K. Developing Capacities of Community Health Workers in Sexual and Reproductive, Maternal, Newborn, Child, and Adolescent Health: A Mapping and Review of Training Resources. PLoS ONE [Internet]. 2014 Apr 15 [cited 2017 Jul 21];9(4). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3988080/

56. Crigler L, Hill K, Furth R, Bjerregaard D. Community Health Worker Assessment and Improvement Matrix (CHW AIM): A Toolkit for Improving Community Health Worker Programs and Services. Revised Version. Published by the USAID Health Care Improvement Project. Bethesda, MD: University Research Co., LLC (URC). 2013.

57. Basic Support for Institutionalizing Child Survival (BASICS) and the Prevention of Postpartum, Hemorrhage Initiative (POPPHI). Training Community Health Workers to Give Maternal and Newborn Health Messages: A Guide for Trainers. Arlington, Va., USA: for the United States Agency for International Development (USAID). 2009.

58. Perry H, Crigler L. Developing and Strengthening Community Health Worker Programs at Scale: a reference guide and case studies for program managers and policymakers. [Internet]. Maternal and Child Health Integrated Program; 2014. Available from: http://www.mchip.net/CHWReferenceGuide

59. Ministerio de Salud. Preparando al Agente COmunitario de Salud para el Cuidado Integral de la Salud y Nutricion de las Gestantes y de las Niñas y Niños Menores de 5 años - “El Manual del Agente Comunitario de Salud.” Ministerio de Salud del Peru; 2009.

60. Ministerio de Salud DG de P de la S. Orientaciones Para El Fortalecimiento de la Labor Del Agente Comunitario de Salud. Ministerio de Salud del Peru; 2014.

61. Organizacion Panamerican de la Salud. Manual del Agente Comunitario de Salud: Manual del Facilitador. Organizacion Mundial de la Salud; 2010.

62. Epi Info™ | CDC [Internet]. 2017 [cited 2018 Sep 13]. Available from: https://www.cdc.gov/epiinfo/index.html

63. ATLAS.ti: The Qualitative Data Analysis & Research Software [Internet]. [cited 2018 Sep 13]. Available from: https://atlasti.com/

16. FIGURE LEGENDS

Figure 1. Theory of Change

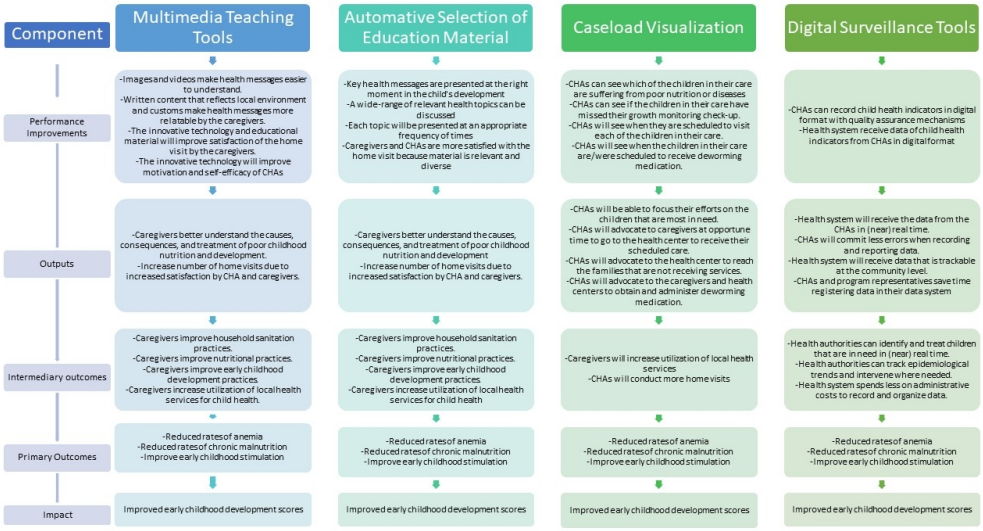


Figure 1

338x190mm (96 x 96 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	___2 and 11___
	2b	All items from the World Health Organization Trial Registration Data Set	__2 and 12____
Protocol version	3	Date and version identifier	__2_____
Funding	4	Sources and types of financial, material, and other support	__12_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	__12_____
	5b	Name and contact information for the trial sponsor	__12_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	__12_____
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	__12_____

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	__2-4_____
	6b	Explanation for choice of comparators	__10-11_____
Objectives	7	Specific objectives or hypotheses	___5_____
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	___5-7_____
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	__5-6_____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	___6_____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	___9-10_____
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	____NA_____
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	___10_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	___NA_____
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	____4-5_____
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	____12-13___

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	__6-7_____
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	___6_____
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	___5_____
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	__NS_____
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	___5_____
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	____NA_____
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	___NA_____
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	__7-11_____
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	____10-11_____

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	_____11___
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	____11_____
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	____NA_____
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	____NA_____
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	___11_____
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	___11_____
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	____NA_____
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	____NA_____
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	___11_____
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	___NA_____

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	___12_____
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	___NA_____
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	___12_____
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	___12_____
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	___12_____
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	___NA_____
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	___12_____
	31b	Authorship eligibility guidelines and any intended use of professional writers	___NA_____
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	___12_____
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	___NA_____
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	___NA_____

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

An mHealth Tool to Improve Community Health Agent Performance for Child Development: Study Protocol for a Cluster-Randomized Controlled Trial in Peru

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-028361.R3
Article Type:	Protocol
Date Submitted by the Author:	25-Sep-2019
Complete List of Authors:	Westgard, Christopher; University of North Carolina at Chapel Hill Gillings School of Global Public Health, Department of Maternal and Child Health; Elementos, Department of Research Rivadeneyra, Natalia; Elementos, Department of Research Mechael, Patricia; HealthEnabled
Primary Subject Heading:	Global health
Secondary Subject Heading:	Health services research, Research methods, Evidence based practice, Health informatics
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, early childhood develoment, Nutrition < TROPICAL MEDICINE, Community child health < PAEDIATRICS, community health worker, Implementation Science

An mHealth Tool to Improve Community Health Agent Performance for Child Development: Study Protocol for a Cluster-Randomized Controlled Trial in Peru

Christopher Westgard[1,2,*]
cmwestgard@unc.edu

Natalia Rivadeneyra[2]
rivadeneyra.natalia@gmail.com

Patricia Mechael[3]
patty@healthenabled.org

1. Department of Maternal and Child Health, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, North Carolina, USA
2. Department of Research, Elementos, Lima, Peru
3. HealthEnabled, Cape Town, South Africa

[*]Corresponding Author:
Jiron Domeyer 105, Barranco, Lima, Peru
cmwestgard@unc.edu
+51.927.980.400

Word Count: 6554

1. ABSTRACT

Introduction: Cultivating child health and development creates long-term impact on the well-being of the individual and society. The Amazon of Peru has high levels of many risk factors that are associated with poor child development. The use of 'community health agents' (CHAs) has been shown to be a potential solution to improve child development outcomes. Additionally, mobile information and communication technology (ICT) can potentially increase the performance and impact of CHAs. However, there is a knowledge gap in how mobile ICT can be deployed to improve child development in low resource settings.

Methods and Analysis: The current study will evaluate the impact of a tablet-based application that intends to improve the performance of CHAs, thus improving the child-rearing practices of caregivers and ultimately child health and development indicators. The CHAs will use the App during their home visits to record child health indicators and present information, images, and videos to teach key health messages. The impact will be evaluated through an experimental cluster randomized controlled trial. The clusters will be assigned to the intervention or control group based on a covariate-constrained randomization method. The impact on child development scores, anemia, and chronic malnutrition will be assessed with an analysis of covariance (ANCOVA). The secondary outcomes include knowledge of healthy child-rearing practices by caregivers, performance of CHAs, and use of health services. The study will be implemented in the Amazon region of Peru with children under 4. The results of the study will provide evidence on the potential of a mHealth tool to improve child health and development indicators in the region.

Ethics and Dissemination: The study received approval from National Hospital "San Bartolome" Institutional Ethics Committee on Nov. 8, 2018 (IRB Approval #15463-18) and will be disseminated via peer-reviewed publications. The trial registration number is ISRCTN43591826.

Keywords: mHealth, ICT, implementation science, impact evaluation, maternal and child health, early childhood development, anemia, malnutrition, community health workers, Peru, Amazon.

2. ARTICLE SUMMARY

2.1. Strengths and Limitations of This Study

- The intermediate variables will be assessed to measure the behavior changes that occurs along the theory of change. The study will be able to evaluate the various mediator variables that are expected to contribute to the final objective.
- A process evaluation with qualitative assessments will be used to identify issues of implementation and inform the implementation plan for scalability.
- The mHealth tool and the monitoring and evaluation strategy provides a surveillance mechanism that will allow for continuous feedback on the use of the intervention tool and health status of the study group.
- Child development will be assessed through a parent reported survey which provides the potential for the parent to give inaccurate responses due to a social desirability bias. However, the instrument that was chosen for the assessment, The CREDI, has shown to have a high correlation to results obtained from surveys that administer direct observation of the child..
- The secondary outcomes that measure changes of the CHAs will be underpowered due to limitations in the sample size of CHAs.

3. BACKGROUND

In low and middle-low income countries millions of children under the age of 5 never reach their cognitive, linguistic and socio-emotional potential (1,2). Chronic malnutrition, anemia and iodine deficiency delay the physical and cognitive development of children, reduce their level of energy,

and weaken their immune system. Child development can also be delayed by low levels of early childhood stimulation (1,3). In the Peruvian Amazon there is a high prevalence of various risk factors associated with developmental delay, especially in rural areas. A study conducted in 2017 showed that the prevalence of developmental delay in the Amazon of Peru was 26.7% (4). In the Amazonian department of Loreto, the prevalence of childhood anemia is 49.9% and chronic malnutrition is 23.6% (2017) (5). Those indicators are worse in indigenous communities (6–9).

The well-being of children in communities can be greatly increased by improving families' understanding of healthy child-rearing practices. Health promotion strategies that establish an intercultural dialogue with families can do a better job at promoting healthy practices than promotion through the health centers (10,11). A program can train and support community members to conduct health promotion that can create behavior changes and improve child development outcomes. Community Health Agents (CHAs) can play an essential role in reducing inequalities in health services by acting as a link between communities and the local health services (11–13). The CHA can establish a warm relationship with the caregiver, thus increasing the acceptance of health advice, improving the absorption of knowledge and getting caregivers involved in the identification and resolution of their own health problems (14–21). The positive impact of CHAs has been associated with a reduction in malnutrition, anemia, malaria, cases of diarrhea, improved child development, and other health indicators (11,22,23). Therefore, understanding and improving the performance of CHAs can greatly improve behavioral outcomes of caregivers, increase the utilization of local health services, and enhance the overall health and well-being of communities (14,24–31).

Several studies have shown that mobile information and communication technology (ICT) can improve the performance of CHAs in their ability to perform health promotion, collect and report timely information regarding family health, provide health services such as vaccines, and refer families to appropriate local health services (32–39). Additionally, when a mobile ICT tool is used by a CHA, the device can increase the confidence the caregivers have in the messages being transmitted and increase the confidence the CHAs have in their own work (32,33,37,38,40,41). Through implementation science, innovations in mobile ICTs and strategies for child health and development can be extended to low resource settings to empower local actors and spread the benefits of advancements in technology (35,36).

A study on the performance of CHAs in the Peruvian Amazon identified difficulties they face in their work. They had difficulty providing a clear explanation of the causes of common diseases and diversifying the health topics that were discussed (29). As described above, an mHealth tool could help the CHAs overcome some of the difficulties they have in conducting an effective home visit. However, there is currently little evidence on the impact of an mHealth tool when used as an educational device by CHAs to improve child development (33). Additionally, there is a knowledge gap on the impact that an mHealth tool can have when utilized by CHAs in rural regions of Peru. Therefore, the present study aims to demonstrate the impact of an mHealth tool used for health promotion and surveillance by CHAs to improve child development in the Peruvian Amazon.

4. HYPOTHESIS

The study hypothesizes that an mHealth tool with educational content developed for the local context will improve the capacity of the CHAs to transmit health messages to the caretakers, thus creating behavior change that will lead to better health and child development outcomes for the children. The hypothesis is based on a theory of change that tracks the mediating variables and considers the potential outputs and outcomes generated by the intervention (42). The theory of change displayed in Figure 1 highlights the various components that are included in the tablet-based application and unfolds the expected outcomes of each. The theory of change is presented

as a comparison to the status-quo; traditional CHA programs in Peru that use paper-based reporting and educational material.

Based on the Theory of Change, the study has the following hypotheses:

H1: The mHealth tool will improve the performance of CHAs during their home visits with children, as measured by doses, content, and inter-personal relationships.

H2: Improved performance by CHAs will increase knowledge acquisition and healthy child-rearing practices by caregivers.

H3: Improved knowledge and healthy practices by caregivers will improve the health and development of the children that receive the intervention.

5. OBJECTIVES

5.1. Main Aim

The objective of the study is to evaluate the impact of the mHealth tool (tablet with application) on child development and nutrition status of children aged 6 to 36 months compared to children who receive home visits from CHA without the mHealth tool.

5.2. Primary Outcomes

1. *[Primary Objective]* Improve child development scores for the children in the intervention group in the domains of language, cognition, gross motor, and social-emotional by 20% compared to the children in the control group ($p<0.05$).
2. Decrease the prevalence of anemia in children by 20% compared to the baseline measurement.
    a. Children in the intervention group will experience a greater reduction in the prevalence of anemia than children in the control group ($p <0.05$)
3. Decrease the prevalence of chronic malnutrition in children by 15%, compared to the baseline measurement.
    a. Children in the intervention group will experience a greater reduction in the prevalence of chronic malnutrition than children in the control group ($p <0.05$).

5.3. Secondary Outcomes

The secondary outcomes of the intervention include indicators of behavior change by CHA and caregivers that have established causal connections with improved health and child development. The intervention is expected to achieve the following secondary outcomes:

4. The caregivers of the intervention group will improve knowledge evaluation scores by 50% compared to the baseline measurement.
5. CHAs in the intervention group will improve their performance evaluation scores by 50% compared to the baseline measurement.
6. More than 50% of the CHAs in the intervention group will express improved satisfaction and self-efficacy when compared to the baseline data.
7. The caregivers of the intervention group will use the local health services for children's health more frequently than they did before baseline.

6. METHODS

6.1. Study Design

The impact will be evaluated through an experimental cluster randomized controlled trial. Each cluster represents a CHA because the children that receive visits from the same CHA must receive the same intervention. Each cluster will be matched with a second cluster using covariate-constrained randomization (43). Recruitment and baseline surveys will be conducted before allocation to the intervention or control group for each cluster. The variables that will be used to covariate-constrained randomization include: the size of the community, type of health facility in the community, distance to the nearest health center (level I-2), and prevalence of anemia. For each cluster pair, one cluster will be randomly assigned to the intervention group and the other to the control group. The covariate-constrained randomization will be conducted with an open-sourced algorithm and the program, R (44).

6.2. Location

The study will be implemented in the Amazon region of Peru. The study will be carried out in the department of Loreto, province of Maynas, and districts of Mazan, Punchana, and Indiana. The district of Mazan has a population of 13,779 (45), a prevalence of chronic malnutrition of 24.4% and a prevalence of anemia at 39.1%, in 2017 (46). The capital of the district of Mazan is located approximately one and a half hours by boat from the capitol city of the province, Iquitos. The district of Punchana has a population of 91,128 (45), a prevalence of chronic malnutrition of 22.7% and a prevalence of anemia of 39.9% (46). The capital of Punchana, is 20 minutes from the city of Iquitos. The district of Indiana has a population of 11,301 (45), a prevalence of chronic malnutrition of 22.4%, and a prevalence of anemia at 46.7%, in 2017(46). The capital of the district of Indiana is 1.5 hours by boat from the city of Iquitos.

The research team with the support of the Regional Ministry of Health of Loreto, will choose the communities that will be included in the study after traveling to the communities to ensure they meet the selection criteria. The study communities must have the following characteristics:

- Has an active CHA that visits families in their community.
- Is not a participant in another health related study.
- Is located less than 6 hours from Iquitos.
- Has at least 25 families and a maximum of 1500 families.

The communities must have an active CHA program for the study because we are measuring the impact of included the mHealth tool in existing CHA programs. The community cannot be participating in another study that includes an intervention that was/will be implemented due to the confounding variables that would created in our study and the other study. The communities must be less than 6 hours from Iquitos due to budgetary restraints that hinder the research team's ability to consistently travel 6 or more hours to execute the study. The size limitation of the community is required to ensure the study obtains the minimum number of children to power the study with the limited number of tablets.

6.3. Participants and Sample Size

The study population includes:

- 10-14 communities, half in the intervention group and half in the control group.
- 40-50 CHAs, half CHAs in the intervention group and half CHAs in the control group.
- 400-450 children, half in the intervention group and half in the control group.

All children between 0 - 36 months in the communities will receive visits from a CHA, in the intervention and control group. However, only the CHAs in the intervention group will receive a tablet with the application to assist their home visits. All the children in the intervention group will have the opportunity to receive the intervention with the tablet.

To assess the impact of the intervention, a sample of the population will be chosen at random to receive the evaluation. The inclusion criteria for the study sample are the following:

- Children who belong to one of the communities included in the study, aged 6 to 36 months.
- Primary caregiver of the child is older than 15 years.
- The caregiver is willing to receive visits from the CHA.

The minimum age of the child to be included in the impact evaluation is determined by the quality of the early childhood development tool. Assessment of child development is more accurate with children older than 5 months (47). The maximum age of the children for the study is determined by the CHA program, which limits home visits by CHAs to children up to 36 months old. The minimum age of the caregiver is 16 because that is the age determined by the communities and the local ethics committee to be capable of giving an informed consent. It is important to capture information from mothers below 18 years old because 39% of the mothers in the region have their first child before the age of 17 (4). Caregivers that do not want to receive visits from CHAs will be excluded because they will not receive the intervention, nor be included in the control group.

The exclusion criteria for the study sample are:

- Families where the main caregiver or the child does not speak Spanish.
- Families that do not want to receive home visits from CHAs.
- Children with mental or physical disabilities.

Families that do not speak Spanish cannot be included because the study does not have appropriate translators for indigenous languages. Children with disabilities will be excluded in the evaluation because the child development evaluation tool is not equipped to evaluate children with these conditions. However, children with disabilities will still receive the intervention.

The sample size for the evaluation is calculated to measure the effect size on the primary outcome indicator, child development. A study in the Amazon region of Peru (2017) determined that the standard deviation of communication scores, determined by the Ages and Stages Questionnaire, was 15.19 (4). The current study predicts a 20% increase in child development scores, which will result in an effect size of 0.49 (average communication score was 37.48, a 20% increase is 44.98, 0.49 standard deviations) (data available in public repository) (4). To calculate the minimal sample size needed, the following parameters were determined:

- Two-sided significance level: 0.05
- Power: 90%
- Effect Size: 0.49
- Avg. Cluster Size: 9
- Intra Cluster Correlation (ICC): 0.15
- Variance Inflation Factor (VIF): 2.2

The following calculation is used to determine the sample size:

$$N \text{ per group} = \frac{[(z_{alpha} + z_{beta})^2 \times 2 \times SD^2]}{\text{Expt'd diff}^2} = \frac{(1.96 + 1.28)^2 \times 2 \times 15.19^2}{(15.19 \times .49)^2}$$

The sample size per group (t-test) with no clusters would be 88. To control for the Intra-Cluster Correlation (ICC), the per group sample size (88) is multiplied by the Variance Inflation Factor (VIF=1+(Avg. Cluster Size–1)*ICC=2.2) to determine the minimal sample size to be **193 per group** (48). The study will include 21 clusters and 9 children and caregivers per cluster.

6.4. **Instruments**

To measure the impact of the intervention and understand the perspective of the users, a series of instruments will be applied to the study participants. The instruments include; evaluation of child development, attitudes and practices questionnaire, knowledge evaluation, performance evaluation of CHAs, and collection of anemia and anthropometric indicators. Qualitative surveys will also be used to evaluate the satisfaction of CHAs and caregivers in relation to the intervention.

The questionnaires and evaluations will be carried out in the homes of the participants. The researcher will ask if a caregiver of a child within the age range is in the home, if so, they will explain the study and ask the caregiver if they want to participant and are willing to sign the informed consent. The researcher will record the responses of the questionnaires and evaluation on a smart phone or electronic tablet.

6.4.1. Evaluation of Child Development

Child development can be effectively evaluated with an instrument that utilizes caregiver-reported data to assess the ability of the child to perform age-relevant developmental activities (47,49–52). The current study will use the Caregiver-Reported Early Development Instrument (CREDI) to evaluate child development (53,54). The CREDI has been validated as an effective instrument to evaluate child development, including low-resource settings in 17 countries (54). The CREDI is effective for large-scale, population-wide studies because it requires less time, materials, and evaluator expertise than other similar instruments (53).

The CREDI is conducted by asking the caregiver if the child is currently capable of completing a list of age-appropriate activities, in which the caregiver can respond by indicating; yes, no, or I don't know. The CREDI will provide a developmental score and a classification that represents the child's development trajectory.. These classifications will be used as the primary dependent variables of the study.

6.4.2. Attitudes and Practices Questionnaire

The study will use a quantitative questionnaire to measure the attitudes and practices of caregivers that influence maternal and child health. The following topics are included in the questionnaire: demographic information, safe pregnancy practices, feeding practices, prevention of illnesses, early childhood stimulation, and use of local health services. The questionnaire will be conducted with all caregivers of the children included in the study. The questionnaire will take approximately 10 minutes.

6.4.3. Knowledge Evaluation

To assess the knowledge of healthy child-rearing practices by the caregiver an instrument was created based on the literature (13,55–57). The Knowledge Evaluation asks the caregiver questions regarding maternal and child health, nutrition, sanitation, and infectious diseases. The questions are open-ended to give the caregiver the opportunity to provide multiple answers that display their knowledge of the topic.

The Knowledge Evaluation will take place directly after the Attitudes and Practices Questionnaire. The Knowledge Evaluation will be scored by giving the participant 1 point for every correct answer they provide. The correct answers will be added together to provide a total "Knowledge Score" for the caregiver.

6.4.4. Performance Evaluation of CHAs

The Performance Evaluation of CHAs was based on an instrument built by the University of West Indies and the Inter-American Development Bank to measure the quality of home visits by CHAs (14). The Performance Evaluation includes questions related to the use of materials, activities, promotion of child development, relationship between CHA and caregivers, and relationships between the CHA and the child. The Performance Evaluation was modified and validated during a previous study in the Amazon region within the local CHA program. The instrument provides further focus on health messages provided by the CHA and the needs of the communities in the Amazon (29).

To conduct the performance evaluation, the researcher will accompany the CHA on their home visit with a child to observe the home visit. The researcher will observe the home visit in silence, trying not to influence the dynamic of the visit. The researcher will take notes during the visit and complete the Performance Evaluation immediately after the conclusion of the home visit.

6.4.5. Survey of the Use of Local Health Services

The research team will survey the local health centers in the communities to obtain statistics regarding the use of health services related to maternal and child health, including: child growth monitoring check-ups, prenatal check-ups, immunization coverage, distribution of micronutrient supplements, distribution of anti-parasitic medicine, and distribution of oral rehydration salts for diarrhea. The survey will be conducted with the nurse that conducts maternal and child health evaluations at the health center. The survey will take approximately 15 minutes and can be filled out independently by the health post representative.

6.4.6. Survey of Child Health Indicators

The CHEST application will be used to collect child health indicators by CHAs during their home visits. The children have a card with information that was recorded during their growth monitoring check-ups at the local health center, including height, weight, age, vaccines, and hemoglobin levels (when tested). The CHA will observe the information written on the card and record it with the application. The CHA will also ask additional questions regarding the health of the child, including incidences of diarrhea, cough, fever, malaria and other illness. The data from the application will be uploaded to the secured server when the CHA or supervisor has access to the cellular network.

6.4.7. Questionnaire on Satisfaction and Self-Efficacy of CHAs

The Questionnaire on Satisfaction and Self-Efficacy of CHAs will be used to measure the degree of satisfaction and self-efficacy the CHAs have from using the CHEST application during their home visits. The questions are both quantitative and qualitative. The CHAs will have the opportunity to describe how the experience with the tablet could be improved.

6.4.8. Questionnaire on Satisfaction of Caregiver

The Questionnaire on Satisfaction of caregivers will be used to measure the degree of satisfaction of the caregivers that received the intervention. The questions are both quantitative and qualitative. The caregivers will have the opportunity to describe what they like and don't like about the use of a tablet during the home visits.

6.5. Patient and Public Involvement

The study was created through formative research done in the same communities to identify their needs and desires related to improving child health and development. A performance evaluation study was conducted with the CHAs in the region by the author (29). In the study, the CHAs and caregivers expressed their need and desire for more information regarding topics of health and child development. The current intervention was created to address those needs.

The results of the study will be presented to the participants, including the community health agents, caregivers, health facility personal, and Regional Ministry of Health in the form of a study brief that indicates the results of each indicator collected. The results will be presented to the public via publication of results in an international scientific journal.

Patients were not involved in the design or recruitment of the study.

7. INTERVENTION

The intervention includes the development and implementation of a tablet-based application (CHEST) to improve the performance of the CHAs during their home visits. The CHAs will use the CHEST Application during their home visits to teach caregivers good health practices and early childhood stimulation. The application will provide the steps for the CHA to follow to conduct an effective home visit. The application will include videos and images to show the caregiver to transmit key health messages. Also, the application will organize the case load of children of the CHA and will provide a mechanism to record maternal and child health indicators.

The intervention is described in the following five phases:

7.1. Phase 1: Preparation of Material

7.1.1. Step-by-Step Agendas for Home Visits

The research team will work with the Regional Ministry of Health of Loreto to build agendas for home visits by the CHAs. The health messages for the home visits are based on national and international manuals for home visits by CHAs to teach maternal and child health and development (58–61). The agendas include steps to follow by the CHA to provide a quality home visit and collect child health indicators. The messages included in the agendas include; what nutritious foods should be consumed by children, how to avoid diarrhea and other diseases, good practices of early attention, and use of health services. There will be 1 agenda for each month of age of the child (1-36 months).

7.1.2. Multimedia Material

The research team will generate multimedia material to be used in the application to transmit health messages. The content will be designed to convey the health messages clearly within the local culture in the Amazon. The material will include videos of people from the region acting out health topics, instructional videos on early childhood stimulation, and animations that describes health issues. In addition, the application will include educational images that have been developed by the regional Ministry of Health of Loreto and other institutions.

7.2. Phase 2: Development of the Application

The research team will evaluate the mHealth applications that have been developed and are open source to determine which will be best to adapt for the current project. The project will contract a team of program developers to modify the open source application to fit the current objectives and local context. The program developer will include the agendas, multimedia, and data collection

mechanisms in the application. The application will function without internet signal and protect all information by password.

7.3. **Phase 3: Baseline Data Collection**

The research team will conduct the surveys and evaluations in the intervention and control communities to obtain a baseline for the study. The instruments that will be applied for the baseline survey include the *Child Development Evaluation, Attitudes and Practices Questionnaire, Knowledge Evaluation, Performance Evaluation of CHA, and Survey on the Use of Health Services*. The baseline survey will be completed before implementation beings in the intervention and control communities.

7.4. **Phase 4: Implementation of Intervention**

7.4.1. Training Workshops

The research team will conduct training workshops with the CHAs in the intervention group to teach them how to use the tablet and application. The workshops will occur during a period of 3 days, 4 hours per day. The leaders of the health facility and Regional Ministry of Health of Loreto will be invited to participate in the workshops and in the supervision of the development of the project.

7.4.2. Distribution of Tablets

After the training workshops, the research team will give a tablet to each CHA in the intervention communities. The CHAs will be instructed to bring the tablet to local health center if they are having problems with the tablet or to store the tablet in their home until a member of the monitoring team visits their community. A supervisor of the CHA program will visit the CHAs to ensure the App is being used and functioning correctly.

7.4.3. The Intervention

The CHAs will continue to conduct home visits with the children in their caseload the same as before the distribution of the tablets. The only change is that the CHAs will use the tablets during the home visits. The number of home visits depends on the demands placed by the community and the motivation of the individual CHA. The CHAs in the communities typically conduct 1-4 home visits per month with children aged 0-36 months. The CHAs are instructed to teach the caregivers good sanitation, nutrition, and child development practices.

The CHAs will use the tablet-based app to visualize the health indicators of the children in their caseload, record health indicators of the child during each visit, observe and chare images and videos that will help teach health and development messaging, and send data to a central database. The App will guide the CHA through each step of the home visit. The supervisor of the CHA program will visit the CHAs to ensure they can upload their data to the database. This include, in some cases, carrying the tablet to a community that has signal to upload the data.

7.4.4. Monitoring

The research team will supervise the work of the CHAs through observations of their home visits and interviews with families and CHAs in the communities. The research team will visit the communities every month during the first 4 months, and less frequently when they see that the program is working as it should.

The team will also track activities of the CHAs through the data uploaded by the application. They will be able to track the number of visits being conducted and the health indicators of the children. If the tablet is not uploading data to the survey, the research team will visit the community to identify the problem.

The local health facility will also have access to the data and will be able to identify if a child is at risk of chronic malnutrition, chronic diarrhea and/or is not attending growth monitoring check-ups.

7.5. **Phase 5: Evaluation of the Intervention**

At the end of the intervention, the follow-up survey will be carried out in the intervention and control communities. The instruments included in the follow-up survey include the *Evaluation of Child Development, Attitudes and Practices Questionnaire, Knowledge Test, Performance Evaluation of CHA, Survey of Use of Health Services, Questionnaire on Satisfaction and Self-Efficacy of CHA*, and *Questionnaire on Satisfaction of Caregivers*.

The data gathered by the application will be used to evaluate the child heath indicators and the number of home visits conducted.

8. DATA ANALYSIS

The quantitative data obtained in the surveys will be organized and analyzed with the statistical software, Epi Info version 7.1.4.0 (62). The qualitative data will be organized and analyzed with the program Atlas.ti (63). To carry out the impact analysis, four mathematical models will be used to interpret the results, generating an optimal analysis to understand the interactions between the variables. The analysis will be conducted on the dependent variable to test the primary outcome, as well as the intermediary variables to test the secondary outcomes and measure the mediating effect of those variables. First, a descriptive analysis will be performed to compare indicators between the analysis groups, including average and frequencies of the independent and dependent variables. Second, a bivariate analysis with Chi-square test will be done to examine the associations between the independent and the dependent variables. Third, a multivariate regression analysis will be used to examine the interactions between the independent variables and the dependent variables. Fourth, an analysis of covariance (ANCOVA) regression method will be used to calculate the impact of the intervention (43).

8.1. **Data Monitoring**

Data monitoring will be completed by the Data Monitoring Committee to ensure non-biased handling and analysis of data obtained from baseline, monitoring, and follow-survey. The Data Monitoring Committee will be made up of the team of experts that will be hired to create the content of the intervention and mentors that guided the research team. The Data Monitoring Committee will each guard files of data at different time points so they can later be crossed reference to ensure consistency. The Data Monitoring Committee will not include permanent members of the sponsor organization or associates of the funding organization or anyone with competing interest or incentive for the intervention to be successful.

8.1. **Data security**

All data will be stored in a secure encrypted server that is protected by password. All identifiable information in the data set will be deleted to make it impossible to link the data with the individual. Information regarding contact information of CHAs will be stored on the secure server. There will be no need to maintain identifies within the data because there will be no follow-up serves with individuals. Members of the Data Monitoring Committee will ensure all identifiable information has been removed from the data set.

9. ETHICS AND DISSEMINATION

The investigation was approved by the Institutional Ethics Committee of the National Hospital "San Bartolomé" in Peru on November 8, 2018 (Exp. Number 15463-18, Oficio N. 0744-2018-OADI-HONADOMANI-SB)

The investigation will include only those individuals that are willing and able to give their consent to be included in the study. The participant must be able to understand the information presented to them and voluntarily express their choice of whether they want to participate or not. The caregivers must be over 15 years of age to participate in the study.

It will be clearly stated that participation in the study will not compromise the health of the participants or violate any rights of the child. There will be no financial compensation for participation in the study. No biological samples will be collected, nor any medical or pharmacological treatments delivered in the research process. There are no possible adverse effects associated with participation in the study. There is the possibility of generating discomfort in the participants because the visits and surveys imply an investment of time. Given this, participants will be informed about the amount of time involved for their participation in the survey before signing the informed consent.

After completion of the child development evaluation the results will be immediately shared with the caretaker along with recommendations of early childhood stimulation activities that could benefit the child. Likewise, the results of the evaluations will be communicated to the health center of the community with a copy of a list of the children who are at risk of developmental delay. The child development evaluation represents a direct benefit to the participants in the intervention and control group.

The research team will monitor the intervention for at least 12 months to ensure the CHAs receive support, and the tablets receive maintenance or are replaced if need. The CHAs can opt-out of the intervention at any time, thus returning to their traditional methods of reporting and health promotion. After 12 months, the program will be handed over to the Municipality and they will continue to receive support as needed. The Municipality has been active in the design of the material for the intervention and will be active in the monitoring and evaluation efforts. The Municipality members will be trained in how to manage and sustain the program.

The results obtained from the study will be made publicly accessible through the publication of findings in an international peer-reviewed journal and a report will be delivered to the local health authorities. The dataset will available in a public data repository.

9.1. Informed consent for caregivers

The Informed Consent for Caregivers includes the description of the study, the participation of the caregiver, the participation of the child, and the amount of time required to complete the survey. The interviewer that conducts the questionnaires will ask for consent from the caregiver. If the caregiver agrees to participate in the study, they will be asked to sign the Informed Consent form. The caregiver will be provided a copy of the consent.

9.2. Informed consent for CHA

The Informed Consent for CHAs includes a description of the study and the performance evaluation that will be conducted with the CHA. The interviewer that conducts the questionnaires will ask for consent from the CHA. If the CHA agrees to participate in the study, they will be asked to sign the Informed Consent for CHAs. The CHA will be offered a copy of the consent.

9.1. Consent to Publish

There will be no identifying images, personal details, or clinical details of participants presented that will compromise the anonymity of the participants in the study.

10.CONCLUSIONS

The results of the study will provide evidence on the potential of a mHealth tool to improve child health and development indicators in the region. The process evaluation with qualitative assessments will also be conducted to identify barriers, strengths, and weaknesses of the program.

11.CHRONOLOGY

The study will last 24 months, beginning in October 2018 and ending in September 2020. The schedule of activities can be found in Table 1.

Table 1: Schedule of Activities

Activity	Oct	Nov	Dec	Jan '19	Feb	Mar	Apr	May	June	July-August	Sep-Dec	Jan-April '20	May-Aug '20
Complete Ethics Committee Protocol													
Develop home visit agendas													
Validate home visit material													
Create videos													
Develop Application													
Validate Application													
Recruit participants													
Baseline Survey													
Train CHAs													
Deploy App													
Monitoring													
Final Evaluation													
End of Project													

11.1. Flow Diagram schedule of activities

The Flow Diagram in Table 2 describes when intervention allocation and assessments of the study population will take place, in relation to the study activities.

Table 2: Flow Diagram

	Study Period				
	Enrolment	Allocation	*Post-Allocation*		*Close-out*
TIMEPOINT	$-t_1$	0	t_1	t_2	t_x
ENROLMENT:					
Eligibility screen of inclusion and exclusion criteria	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
Distribution of Tablet			←	—	→

Control group			←	—	→
ASSESSMENTS:					
Child development evaluation	X				X
Performance Evaluation	X				X
Knowledge, Attitudes, and Practices Survey	X				X
Monitoring of Community Health Agents		X	X	X	

12.ABBREVIATIONS

CHA – community health agents
CHEST – Child Health Education and Surveillance Tool
CREDI – Caregiver-Reported Early Development Instrument
ICT – Information and communication technology

13. DECLARATIONS

13.1. Availability of data and materials

The datasets generated during the study will be stored in the publicly available repository, figshare (https://figshare.com/). De-identified participant data, including child development evaluation scores, anemia results, chronic malnutrition results, KAP survey results, and CHA performance evaluations, will be stored in the repository. The data will be available through the repository for 10 years. Data from participants will only be made available if consent was provided by the participant through the informed consent process.

13.2. Competing interests

The authors and members of the research team have no competing interest.

13.3. Communication of Trial Results

The results of the study will be presented to the participants, including the community health agents, caregivers, health facility personal, and Regional Ministry of Health in the form of a study brief that indicates the results of each indicator collected. The study brief will be written and described in a manner that is intelligible for the target population. The CHAs will be asked to distribute the brief and describe the findings to the individual families in their caseload.

The results will be presented to the public via publication of results in an international scientific journal. The research team will also seek opportunities to present the results in national and international conferences to disseminate findings.

13.4. FUNDING

The study is funded by the grant, Saving Brains, by Grand Challenges, Canada. The funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

13.5. AUTHOR CONTRIBUTIONS

CW conceived of the study. CW and NR contributed to the writing and revision of the protocol. PM provided advisory on study design. All authors contributed to refinement of the study protocol and approved the final manuscript.

13.6. **ACKNOWEDGEMENTS**

Special thanks to Liz Franco, Luis Orrego Ferreyros, Milagros Alvarado Llatance, and Gabriela Palacios Rojo for their assistance in developing the material and instruments of the study. Thanks to the Ministry of Development and Social Inclusion of Peru for their collaboration in designing the tool and identifying the participants and recipients of the study. Special thanks to Grand Challenges Canada for providing advisory service regarding study design, implementation strategies, and strategies to scale the intervention.

14.TRIAL SPONSOR

Trial Sponsor: Elementos
Contact Name: Christopher Westgard
Address: Jiron Domeyer, Barranco, Lima, Peru
Telephone: +51927980400
Email: cmwestgard@unc.edu

15. REFERENCES

1. Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B. Developmental potential in the first 5 years for children in developing countries. The Lancet. 2007 Jan 6;369(9555):60–70.

2. Engle PL, Black MM, Behrman JR, Mello MC de, Gertler PJ, Kapiriri L, et al. Strategies to avoid the loss of developmental potential in more than 200 million children in the developing world. The Lancet. 2007 Jan 20;369(9557):229–42.

3. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. Lancet Lond Engl. 2011 Oct 8;378(9799):1325–38.

4. Westgard C, Alnasser Y. Developmental delay in the Amazon: The social determinants and prevalence among rural communities in Peru. PloS One. 2017;12(10):e0186263.

5. Instituto Nacional de Estadistica e Informatica. Loreto Compendio Estadistico 2017. Sistema Estadistico Nacional; 2017.

6. Anticona C, San Sebastian M. Anemia and malnutrition in indigenous children and adolescents of the Peruvian Amazon in a context of lead exposure: a cross-sectional study. Glob Health Action. 2014;7:22888.

7. Díaz A, Arana A, Vargas-Machuca R, Antiporta D. Situación de salud y nutrición de niños indígenas y niños no indígenas de la Amazonia peruana. US11 [Internet]. 2015 [cited 2017 Jan 26]; Available from: http://iris.paho.org/xmlui/handle/123456789/10008

8. Flores-Bendezu J, Calderon J, Rojas B, Alarcon-Matutti E, Gutierrez C. Chronic malnutrition and anemia in children under 5 years of indigenous households of Peru - Analysis of Demographic and Health Survey 2013. Fac Med 2015762135-40 Dxdoiorg1015381analesv76i211139.

9. Grantham-McGregor SM, Fernald LCH, Kagawa RMC, Walker S. Effects of integrated child development and nutrition interventions on child development and nutritional status. Ann N Y Acad Sci. 2014 Jan;1308:11–32.

10. Perry HB, Sacks E, Schleiff M, Kumapley R, Gupta S, Rassekh BM, et al. Comprehensive review of the evidence regarding the effectiveness of community–based primary health care in improving maternal, neonatal and child health: 6. strategies used by effective projects. J Glob Health [Internet]. [cited 2017 Nov 9];7(1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5491945/

11. Gilmore B, McAuliffe E. Effectiveness of community health workers delivering preventive interventions for maternal and child health in low- and middle-income countries: a systematic review. BMC Public Health. 2013 Sep 13;13:847.

12. Global Health Workforce Alliance, World Health Organization. Global experience of community health workers for delivery of health related millennium development goals: a systematic review, country case studies, and recommendations for integration into national health systems. 2010.

13. The Earth Institute. Millennium Villages Project. Community Health Worker Trainer's Manual. A guide to Home Based Services [Internet]. Version 2.1. Columbia University; 2013. Available from: http://millenniumvillages.org/wp-content/uploads/2014/09/CHWTrainingManual.pdf

14. Leer J, Lopez-Boo F, Perez Exposito A, Powell C. A Snapshot on the Quality of Seven Home Visit Parenting Programs in Latin America and the Caribbean. Inter-American Development Bank; 2016.

15. Schodt S, Parr J, Maria CA, Rubio-Codina M. La medición de la calidad de os servicios de visitas domiciliarias . Una revisión de la literatura. Danco Interamericano de Desarrollo; 2015.

16. Vogel CA, Caronongan P, Thomas J, Bandel E, Xue Y, Henke J, et al. Toddlers in Early Head Start: A Portrait of 2-Year-Olds, Their Families, and the Programs Serving Them. Volume 1: Age 2 Report. OPRE Report 2015-10 [Internet]. Administration for Children & Families; 2015 [cited 2017 Aug 3]. Available from: https://eric.ed.gov/?id=ED558558

17. Roggman LA, Cook GA, Innocenti MS, Jump Norman V, Boyce LK, Christiansen K, et al. Home Visit Quality Variations in Two Early Head Start Programs in Relation to Parenting and Child Vocabulary Outcomes. Infant Ment Health J. 2016 May 1;37(3):193–207.

18. Medina A, Sofía I. Evaluation protocol application of tasks for the socio - cognitive development in children from 37 to 71 months in the Program of Comprehensive Attention to Early Childhood Modality Family Environment District Secretariat of Social Integration [Internet]. [cited 2017 Aug 3]. Available from: https://intellectum.unisabana.edu.co/handle/10818/23587

19. Fernández S, Yonah R. Aplicación de ensayos domiciliarios para evaluar la adopción de prácticas mejoradas de alimentación complementaria en madres. Centro materno infantil Juan Pablo II. Villa El Salvador, Lima. 2005. Univ Nac Mayor San Marcos [Internet]. 2007 [cited 2017 Aug 4]; Available from: http://cybertesis.unmsm.edu.pe/handle/cybertesis/1121

20. Walker SP, Powell C, Chang SM, Baker-Henningham H, Grantham-McGregor S, Vera-Hernandez M, et al. Estrategias de apoyo parental a través de los servicios de salud en el Caribe [Internet]. BID; 2016 Feb [cited 2017 Aug 3]. Available from: http://repositorio.minedu.gob.pe/handle/123456789/4112

21. Chang-Say Chong A. La comunicación en los proyectos de lucha contra la desnutrición crónica infantil : el caso Ally Micuy (Áncash). Pontif Univ Católica Perú [Internet]. 2014 Sep 25 [cited 2017 Aug 3]; Available from: http://tesis.pucp.edu.pe/repositorio/handle/123456789/5598

22. Lewin S, Munabi-Babigumira S, Glenton C, Daniels K, Bosch-Capblanch X, Wyk BE van, et al. Lay health workers in primary and community health care for maternal and child health and the management of infectious diseases. Cochrane Database Syst Rev [Internet]. 2010 [cited 2018 Sep 19];(3). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004015.pub3/abstract

23. Lassi ZS, Kumar R, Bhutta ZA. Community-Based Care to Improve Maternal, Newborn, and Child Health. In: Black RE, Laxminarayan R, Temmerman M, Walker N, editors. Reproductive, Maternal, Newborn, and Child Health: Disease Control Priorities, Third Edition (Volume 2) [Internet]. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2016 [cited 2016 Jun 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK361898/

24. Howard KS, Brooks-Gunn J. The role of home-visiting programs in preventing child abuse and neglect. Future Child. 2009;19(2):119–46.

25. Singh V, Ahmed S, Dreyfuss ML, Kiran U, Chaudhery DN, Srivastava VK, et al. Non-governmental organization facilitation of a community-based nutrition and health program: Effect on program exposure and associated infant feeding practices in rural India. PloS One. 2017;12(9):e0183316.

26. Swider SM. Outcome Effectiveness of Community Health Workers: An Integrative Literature Review. Public Health Nurs. 2002 Jan 1;19(1):11–20.

27. Agarwal S, Perry HB, Long L-A, Labrique AB. Evidence on feasibility and effective use of mHealth strategies by frontline health workers in developing countries: systematic review. Trop Med Int Health TM IH. 2015 Aug;20(8):1003–14.

28. Mobile Healthcare Information for All. Assessment of mHealth applicaitons for their potential to provide essential healthcare information for citizens in low resource settings. HIFA; 2017.

29. Westgard C, Naraine R, Paucar Villacorta DM. Performance Evaluation of Community Health Workers: Case Study in the Amazon of Peru. J Community Health. 2018 Mar 26;

30. Ballard M, Montgomery P. Systematic review of interventions for improving the performance of community health workers in low-income and middle-income countries. BMJ Open. 2017 Oct 1;7(10):e014216.

31. Cometto G, Ford N, Pfaffman-Zambruni J, Akl EA, Lehmann U, McPake B, et al. Health policy and system support to optimise community health worker programmes: an abridged WHO guideline. Lancet Glob Health. 2018 Dec 1;6(12):e1397–404.

32. Ilozumba O, Dieleman M, Kraamwinkel N, Belle SV, Chaudoury M, Broerse JEW. "I am not telling. The mobile is telling": Factors influencing the outcomes of a community health worker mHealth intervention in India. PLOS ONE. 2018 Mar 27;13(3):e0194927.

33. van Heerden A, Sen D, Desmond C, Louw J, Richter L. App-Supported Promotion of Child Growth and Development by Community Health Workers in Kenya: Feasibility and Acceptability Study. JMIR MHealth UHealth [Internet]. 2017 Dec 5 [cited 2018 Sep 19];5(12). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5736876/

34. Lee S, Chib A, Kim J-N. Midwives' Cell Phone Use and Health Knowledge in Rural Communities. J Health Commun. 2011 Oct 1;16(9):1006–23.

35. Peterson HB, Haidar J, Fixsen D, Ramaswamy R, Weiner BJ, Leatherman S. Implementing Innovations in Global Women's, Children's, and Adolescents' Health: Realizing the Potential for Implementation Science. Obstet Gynecol. 2018 Mar;131(3):423–30.

36. Peterson HB, Haidar J, Merialdi M, Say L, Gülmezoglu AM, Fajans PJ, et al. Preventing maternal and newborn deaths globally: using innovation and science to address challenges in implementing life-saving interventions. Obstet Gynecol. 2012 Sep;120(3):636–42.

37. Källander K, Tibenderana JK, Akpogheneta OJ, Strachan DL, Hill Z, Asbroek AHA ten, et al. Mobile Health (mHealth) Approaches and Lessons for Increased Performance and Retention of Community Health Workers in Low- and Middle-Income Countries: A Review. J Med Internet Res. 2013;15(1):e17.

38. Prinja S, Nimesh R, Gupta A, Bahuguna P, Gupta M, Thakur JS. Impact of m-health application used by community health volunteers on improving utilisation of maternal, new-born and child health care services in a rural area of Uttar Pradesh, India. Trop Med Int Health TM IH. 2017;22(7):895–907.

39. Ilozumba O, Van Belle S, Dieleman M, Liem L, Choudhury M, Broerse JEW. The Effect of a Community Health Worker Utilized Mobile Health Application on Maternal Health Knowledge and Behavior: A Quasi-Experimental Study. Front Public Health [Internet]. 2018 May 7 [cited 2019 Apr 30];6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5949315/

40. Chib A. The Aceh Besar midwives with mobile phones project: Design and evaluation perspectives using the information and communication technologies for healthcare development model. J Comput-Mediat Commun. 2010 Apr 1;15(3):500–25.

41. Limaye NP, Rivas-Nieto AC, Carcamo CP, Blas MM. Nuestras Historias- Designing a novel digital story intervention through participatory methods to improve maternal and child health in the Peruvian Amazon. PLOS ONE. 2018 Nov 5;13(11):e0205673.

42. Lafferty CK, Mahoney CA. A Framework for Evaluating Comprehensive Community Initiatives. Health Promot Pract. 2003 Jan 1;4(1):31–44.

43. Ivers NM, Halperin IJ, Barnsley J, Grimshaw JM, Shah BR, Tu K, et al. Allocation techniques for balance at baseline in cluster randomized trials: a methodological review. Trials. 2012 Aug 1;13(1):120.

44. Carter BR, Hood K. Balance algorithm for cluster randomized trials. BMC Med Res Methodol. 2008 Oct 9;8(1):65.

45. Instituto Nacional de Estadistica E Informatica. Estadisticas. Poblacion y Vivienda. Poblacion Ttoal al 30 de Junio, POr Grupos Quinquenales de Edad, Segun Departamento, Provincia y Distrito, 2015 [Internet]. 2015. Available from: https://www.inei.gob.pe/estadisticas/indice-tematico/poblacion-y-vivienda/

46. Instituto Naciona De Salud. Sistema de informacion del estado nutricional (SIEN). 2017 [Internet]. Available from: https://web.ins.gob.pe/es/alimentacion-y-nutricion/vigilancia-alimentaria-y-nutricional/vigilancia-del-sistema-de-informacion-del-estado-nutricional-en-%20EESS

47. Rubio-Codina M, Araujo MC, Attanasio O, Muñoz P, Grantham-McGregor S. Concurrent Validity and Feasibility of Short Tests Currently Used to Measure Early Childhood Development in Large Scale Studies. PLOS ONE. 2016 Aug 22;11(8):e0160962.

48. Kelsey J, Whittemore A, Evans A, Thompson D. Methods in Observational Epidemiology. Monographs in Epidemiology and Biostatistics. Second Edition. Vol. 26. New York: Oxford University Press; 1996.

49. Fernald LCH, Kariger P, Hidrobo M, Gertler PJ. Socioeconomic gradients in child development in very young children: evidence from India, Indonesia, Peru, and Senegal. Proc Natl Acad Sci U S A. 2012 Oct 16;109 Suppl 2:17273–80.

50. Fernald L, Kariger P, Engle P, Raikes A. Examining Early Child Development in Low-Income Countries: A Toolkit for the Assessment of Children in the First Five Years of Life. The World Bank; 2009.

51. Rubio-Codina M, Araujo MC, Attanasio O, Grantham-McGregor S. Validez concurrente y viabilidad de pruebas cortas comunmente usadas para medir el desarrollo infantil temprano en estudios a gran escala: Metodologia y resultados. Banco Interam Desarro [Internet]. 2016 Agosto;(723). Available from: https://publications.iadb.org/bitstream/handle/11319/7823/Validez-concurrente-y-viabilidad-de-pruebas-cortas-comunmente-usadas-para-medir-el-desarrollo-infantil-temprano-en-estudios-a-gran-escala-metodologia-y-resultados.pdf

52. Rubio-Codina M, Attanasio O, Grantham-McGregor S. Mediating pathways in the socio-economic gradient of child development: Evidence from children 6–42 months in Bogota. Int J Behav Dev. 2016 Nov 1;40(6):483–91.

53. McCoy DC, Waldman M, Fink G. Measuring early childhood development at a global scale: Evidence from the Caregiver-Reported Early Development Instruments. Early Child Res Q. 2018 Oct 1;45:58–68.

54. McCoy DC, Fink G, Pierre-Louis M. CREDI. Caregiver-Reported Early Development Instruments. User Guide. [Internet]. 2018. Available from: sites.sph.harvard.edu/credi/

55. Tran NT, Portela A, de Bernis L, Beek K. Developing Capacities of Community Health Workers in Sexual and Reproductive, Maternal, Newborn, Child, and Adolescent Health: A Mapping and Review of Training Resources. PLoS ONE [Internet]. 2014 Apr 15 [cited 2017 Jul 21];9(4). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3988080/

56. Crigler L, Hill K, Furth R, Bjerregaard D. Community Health Worker Assessment and Improvement Matrix (CHW AIM): A Toolkit for Improving Community Health Worker Programs and Services. Revised Version. Published by the USAID Health Care Improvement Project. Bethesda, MD: University Research Co., LLC (URC). 2013.

57. Basic Support for Institutionalizing Child Survival (BASICS) and the Prevention of Postpartum, Hemorrhage Initiative (POPPHI). Training Community Health Workers to Give Maternal and Newborn Health Messages: A Guide for Trainers. Arlington, Va., USA: for the United States Agency for International Development (USAID). 2009.

58. Perry H, Crigler L. Developing and Strengthening Community Health Worker Programs at Scale: a reference guide and case studies for program managers and policymakers. [Internet]. Maternal and Child Health Integrated Program; 2014. Available from: http://www.mchip.net/CHWReferenceGuide

59. Ministerio de Salud. Preparando al Agente COmunitario de Salud para el Cuidado Integral de la Salud y Nutricion de las Gestantes y de las Niñas y Niños Menores de 5 años - “El Manual del Agente Comunitario de Salud.” Ministerio de Salud del Peru; 2009.

60. Ministerio de Salud DG de P de la S. Orientaciones Para El Fortalecimiento de la Labor Del Agente Comunitario de Salud. Ministerio de Salud del Peru; 2014.

61. Organizacion Panamerican de la Salud. Manual del Agente Comunitario de Salud: Manual del Facilitador. Organizacion Mundial de la Salud; 2010.

62. Epi Info™ | CDC [Internet]. 2017 [cited 2018 Sep 13]. Available from: https://www.cdc.gov/epiinfo/index.html

63. ATLAS.ti: The Qualitative Data Analysis & Research Software [Internet]. [cited 2018 Sep 13]. Available from: https://atlasti.com/

16. FIGURE LEGENDS

Figure 1. Theory of Change

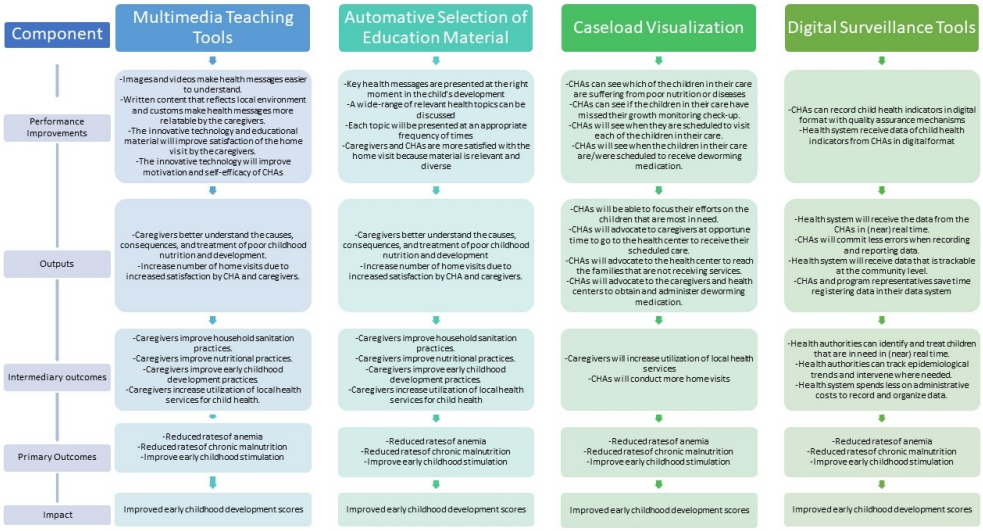


Figure 1

338x190mm (96 x 96 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	___2 and 11___
	2b	All items from the World Health Organization Trial Registration Data Set	__2 and 12____
Protocol version	3	Date and version identifier	__2_____
Funding	4	Sources and types of financial, material, and other support	__12_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	__12_____
	5b	Name and contact information for the trial sponsor	__12_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	__12_____
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	__12_____

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	__2-4_____
	6b	Explanation for choice of comparators	__10-11_____
Objectives	7	Specific objectives or hypotheses	___5_____
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	___5-7_____
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	__5-6_____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	___6_____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	___9-10_____
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	____NA_____
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	___10_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	___NA_____
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	____4-5_____
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	____12-13___

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	__6-7_____
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	___6_____
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	___5_____
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	__NS_____
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	___5_____
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	____NA_____
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	___NA_____
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	__7-11_____
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	____10-11_____

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	_____11___
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	____11_____
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	____NA_____
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	____NA_____
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	___11_____
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	___11_____
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	____NA_____
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	____NA_____
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	___11_____
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	___NA_____

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	___12_____
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	___NA_____
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	___12_____
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	___12_____
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	___12_____
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	___NA_____
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	___12_____
	31b	Authorship eligibility guidelines and any intended use of professional writers	___NA_____
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	___12_____
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	___NA_____
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	___NA_____

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.