Title: Mobile Health Intervention to Promote Positive Infant Health Outcomes in Guatemala

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Wuqu' Kawoq | Maya Health Alliance (Maya Health Alliance or MHA)
Protocol Summary Form

NAME OF PRINCIPAL INVESTIGATOR:

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PROTOCOL TITLE: Mobile Health to Promote Positive Infant Outcomes in Guatemala

SOURCE OF FUNDING: United States National Institutes of Health

SPECIFIC AIMS:
(State objectives concisely, describe hypothesis tested)

Investments made early in the life course—especially efforts directed at supporting development in the first two years of life—are more cost-effective than interventions later in childhood and can permanently enhance development (5-9). Consequently, one of the most effective and evidence-based interventions for ensuring healthy child development is the promotion of high-quality, nurturing care by primary caregivers in the first months of life (10) (See Table 1).

Table 1

STUDY AIMS			
	Aim 1	**Aim 2**	**Aim 3**
Study Design	Prospective single visit or repeated visit small group interviews	Two-arm prospective, longitudinal, randomized, 6-month pilot intervention to assess the implementation characteristics of the technology—usability, acceptability, and sustainability. Outcomes assessed at 6 months.	Two-arm prospective, longitudinal, randomized 18-month intervention with developmental outcomes assessed at 18 months to help determine the effectiveness of a smartphone-based, real-time caregiver feedback intervention.
Study Procedures	Focus groups	The intervention arm (n=20) will receive the smartphone application. The control arm (n=20) will receive printed caregiving materials.	The intervention arm (n=110) will receive the smartphone application. The control arm (n=110) will receive printed caregiving materials.
Recruitment	Up to 20 caregivers and up to 20 Maya Health Alliance staff will be recruited for formative focus groups	40 caregivers and their infants from birth to 4 weeks of age	220 first-time caregivers and their infants from birth to 4 weeks of age

Duration	Focus groups will be 1-2 hours in duration.	6 months with 7 home visits by research staff (initial visit and monthly follow-up visits months 1-6)	18 months with 8 home visits by research staff (initial visit, follow-up visits every 3 months and 1 visit at the end of the study for BSID 4).
Outcome Measures	To develop a new mHealth smartphone application to engage primary caregivers directly in the active monitoring of their infants' development, and to provide tailored feedback and support for the provision of nurturing care.	To collect data on usability and acceptability of the technology to end users and determine effect size of clinical effectiveness (infant development outcomes). The primary outcome is BSID-4 as a measure of infant developmental outcomes.	To test clinical effectiveness (improved infant development outcomes and caregiving behaviors). The primary outcome is BSID-4 as a measure of infant developmental outcomes. The secondary outcomes are quality of infant-caregiver interaction (NCAST feeding scale) and quality of the home environment (HOME scale).

- In Aim 1, we will develop a new mHealth smartphone application which can be used to engage primary caregivers directly in the active monitoring of their infants' development, and to provide tailored feedback and support for the provision of nurturing care. Aim 1 will use focus groups, an Agile Design process, and the RE-AIM framework for assessment.
- In Aim 2, we will prospectively assess the implementation characteristics of the technology—usability, acceptability, and sustainability—for caregivers over time for different periods of infant development. Aim 2 will use a prospective, longitudinal, six-month pilot intervention, enrolling 40 caregivers and their infants from birth to 4 weeks of age (using simple randomization to assign them to either the 6-month smartphone intervention (n=20) or control (receipt of printed parenting materials, n=20).
- Aim 3 is similar to Aim 2 only 1) it is adequately powered based on Aim 2 results with 110 participants per group, 2) the developmental outcome (BSID-4) will be measured at 18 months in Aim 3 instead of 6 months in Aim 2, and 3) we will add assessment of quality of infant-caregiver interaction as measured by the Nursing Child Assessment Satellite Training (NCAST) feeding scale and Home Observation for the Measurement of the Environment (HOME scale).

BACKGROUND AND SIGNIFICANCE:
(Brief paragraph summarizing any information important for understanding the study and proposed research procedures)

According to recent estimates, 43% of children under age 5 residing in low- and middle-income countries (LMICs)—250 million children in total—are at risk of not reaching their developmental potential due to living in environments with malnutrition, poverty, and lack of early stimulation. (3-5) Most community programs rely on basic growth indicators or parent-reported concerns, techniques which are indirect measures of development and not sensitive in infancy. As a result, data on the onset of developmental disabilities in infants are almost completely missing, and early interventions are begun well after significant effects have already occurred. Technologies to support earlier identification of atypical development would therefore support earlier intervention and improved neurodevelopmental outcomes.

Numerous studies in LMICs have intervened with caregivers to promote infant development. However, most have involved face-to-face interactions between frontline staff--usually community health workers--and caregivers (6,11-14). While this is an effective strategy, it may cause health system strain, as it relies on health workers who have many competing demands on their time. This “task-shifting” can lead to overburdening and deterioration of intervention quality (15-18). For infant development, mHealth technologies have the potential to solve this problem by providing tailored content directly to caregivers, involving and empowering them to promote infant development, promoting and facilitating interactions with health workers when areas of concern are identified and, therefore, expanding the reach of healthcare systems.

This project will use mHealth to provide caregiver feedback and anticipatory guidance around three key infant caregiving domains: sleep, feeding, and activity/caregiver interaction. For each of these domains, evidence-based international guidelines exist, published by the World Health Organization (WHO) and UNICEF (63). Recent efforts by our team have included cultural adaptations of these guidelines to Guatemala, including UNICEF/WHO/s Care for Child Development (63). These adapted caregiver recommendations will form the basis for the content to be incorporated into the smartphone app during this project.

The purpose of this Android app is to provide general anticipatory age-based guidance to caregivers in Guatemala on infant growth, nutrition, sleep, and development. The app is intended to increase patient awareness, education, and empowerment, and support patient-centered health-care. The app is not intended for use in the diagnosis of diseases or conditions, or in the cure, mitigation, treatment, or prevention of disease by aiding clinical decision making. Reinforcing feedback based on the entered data will be provided via direct interaction (by phone/text) with health workers from Maya Health Alliance for problem areas. No data will be used clinically. The intended users of the app are caregivers in rural Guatemala. The app uses a standard Android registration workflow. A caregiver (end user) registers using their name and a password. Either preferred phone number or email is also collected to assist the end user with password recovery if they forget their password. After registering as a user, the caregiver (end user) can then enter their infant child's information into the app (name, sex, date of birth). Data collected on the app will sync to a secure cloud-based server backend at the project partner Wuqu' Kawoq in Guatemala. Only implementing staff at Wuqu' Kawoq have

direct access to this data. Deidentified data (i.e. survey responses)from the server will be shared by Wuqu' Kawoq staff with the study team. Information from the mobile app will not be placed in medical records. The mobile app will be available in Spanish and not in Kaqchikel since this language is mostly an oral language read by very few.

RESEARCH DESIGN AND METHODS:

(Briefly describe study design, anticipated enrollment, eligibility criteria, study procedures. If study involves a medical intervention, describe standard of care and how study procedures differ from standard of care. Explicitly describe how risk to subjects is being minimized. Explicitly describe methods being used to ensure subject safety, including criteria for removing a subject from the study if applicable)

Study Design:

This research will be conducted in Tecpán, Guatemala where Wuqu' Kawoq | Maya Health Alliance has its main clinical office.

Aim 1 Study Design: Prospective single visit or repeated visit small group interviews. We will conduct focus groups to gather end-user perspectives on a smartphone application to support caregivers.

Aim 2 Study Design. Two-arm prospective, longitudinal, randomized 6-month pilot intervention. We will assess the implementation characteristics of the smartphone application through a longitudinal, six-month usability trial, to determine caregiver engagement over time and to assess the perceived usefulness of the application. Aim 2 will complement the technical work in Aim 1 by conducting a larger-scale pilot implementation of the caregiver smartphone application. Aim 2 is designed to collect data on usability and acceptability of the technology to end users and determine effect size of clinical effectiveness (infant development outcomes).

Aim 3 Study Design. Two-arm prospective, longitudinal, randomized 18-month intervention with developmental outcomes assessed at 18 months. Aim 3 will determine the effectiveness of a smartphone-based, real-time caregiver feedback intervention to promote positive infant developmental outcomes and improved caregiving behaviors. Aim 3 will test clinical effectiveness (improved infant development outcomes and caregiving behaviors).

Eligibility criteria:

Criteria for all aims of the study will be as follows:

> Inclusion Criteria: Consenting first-time caregivers with an infant in the eligible age range (0-4 weeks), singleton, full-term (>37 weeks) birth. For stakeholder interviews and application testing phases, any consenting caregiver with an infant less than 6 months of age and a smartphone, or any Maya Health Alliance staff member who works with infants will be eligible to participate.

Exclusion Criteria: Presence of acute malnutrition/wasting or severe medical illness (heart disease, kidney disease, congenital abnormality), medical need for supplementation of breastfeeding, caregiver not literate (our exploratory feasibility data in preparation for this proposal shows that >95% of first time caregivers in the region are now literate).

Recruitment:

The caregivers participating in both phases (Aim 1, design/formative phase; Aim 2, implementation/trial phase) will be recruited from among first-time caregivers receiving services at a major maternal-child wellness clinic run by Maya Health Alliance out of their main office in Tecpán Guatemala.

For Aim 1, up to 20 caregivers will be recruited in this fashion for formative focus groups. Up to 20 Maya Health Alliance staff will be recruited. All staff who work in early child development and nutrition programs will be eligible. Recruitment will be by word of mouth.

These participants will then be invited, as they are willing, to participate in the formative agile design phase of the app. Subsequently, in Aims 2 and 3, 40 and 220 (respectively) additional caregiver/infant dyads will be recruited in the same fashion into participate in the prospective implementation trial.

Study Procedures:

Aim 1: Focus groups: User perspectives will be collected using a focus group format, facilitated by a research staff at Maya Health Alliance under the supervision of Dr. Rohloff, who is fluent in Spanish and Kaqchikel Maya, so that speakers who prefer either language can be included. Convenience samples of caregivers who own smartphones and have infants 0-6 months old will be recruited from Maya Health Alliance clinics, taking care to recruit both male and female caregivers. These will be supplemented by additional focus groups with Maya Health Alliance early child development staff (nurses, technicians, physicians). Four focus groups (1-2 hours in duration) will be conducted, with 5-10 participants each (2 groups caregivers, 2 groups staff). Additional focus groups, up to 5 total, will be held as needed so that preference can be given to those who prefer to conduct the sessions in Spanish or Kaqchikel. During the focus groups, participants will be asked about their opinions around their experience with smartphone applications and understanding of an mHealth application in supporting caregiving. Participants will also be shown and have the opportunity to work with examples of existing parenting/caregiving applications and will be asked to provide feedback on the usefulness of these existing applications.

Aim 2: Two-arm prospective, longitudinal, randomized 6-month pilot intervention. Recruited caregivers/infants will undergo simple randomization to one of 2 arms. The control arm (n=20) will receive printed caregiving materials based on recommendations outlined in Table 2. The intervention group (n=20) will receive the

smartphone application. Study staff will make an initial home visit (less than an hour) to install the application on the caregiver phone and demonstrate use and collect baseline data. The baseline data will include: infants/caregivers demographics, poverty scorecard, infant's pre- and post-natal medical history and anthropometrics. The baseline data will be collected using an electronic RedCap form. "Teach back" demonstration will be used to assure understanding. Subsequently, in the intervention arm, staff will make monthly visits (approximately 15 minutes duration) to assess functionality of the smartphone and answer questions/reinforce use. In the control arm, staff will make monthly visits (approximately 15 minutes duration) to ask if there are questions about the printed caregiving materials. The smartphone app in the intervention arm will function as follows. On 3 consecutive days per week it will query caregivers to complete a 20-second survey that asks about 1) frequency, amount and type of feeding, 2) frequency and duration of sleeping, or 3) frequency, duration and type of activity and interaction, subsequently providing reinforcing feedback based on entered data and permitting direct interaction (by phone/text) with health workers from Maya Health Alliance for problem areas identified as described above. On non-survey days, the app will provide age-based anticipatory guidance (Table 2). For the 6-month study, there will be a total of 9 visits. The study will last 6 months and consist of 7 home visits by research staff (initial visit and monthly follow-up visits months 1-6) and 2 BSID-4 assessment visits (at baseline and conclusion). The BSID-4 can be completed in a space provided by the institution or close to where the subject lives to ensure comfort for their child. During the home visits, research staff will also collect the following information from all subjects (intervention and control): Infant/caregiver demographics (first visit), infant's medical history (first visit), caregiver poverty scorecard (first visit), infant's height and weight (each visit) For the intervention arm, app usability (*System Usability Scale Survey)* and usefulness and satisfaction (*Usefulness and Satisfaction Survey*) scales will be done at the first and last visit. These surveys will be collected using an electronic RedCap form. This information will be collected for research purposes only and will be obtained directly from the caregiver. The BSID-4 will be measured at enrollment and study conclusion during a separate assessment visit (less than an hour in duration). A semi-structured interview with subjects enrolled in the intervention group at the last visit will be used to qualitatively assess interest, engagement, and perceptions of the app technology. This interview will be audio-recorded to accurately capture each subjects response. The audio-recordings will not be shared outside the research team and will be destroyed once they have been transcribed.

Aim 3: Two-arm prospective, longitudinal, randomized 18-month intervention with developmental outcomes assessed at 18 months. Recruited caregivers/infants will undergo simple randomization to one of 2 arms. The control arm will receive printed caregiving materials based on recommendations outlined in Table 1. The intervention group will receive the smartphone application. Study staff will make an initial home visit (less than an hour) to install the application on the caregiver phone and demonstrate use. "Teach back" demonstration will be used to assure understanding.

Subsequently, in the intervention arm, staff will make visits every 3 months (less than 1 hour duration) to assess functionality of the smartphone and answer questions/reinforce use.

In the control arm, staff will conduct visits every 3 months (less than 1 hour duration) to ask if there are questions about the printed caregiving materials. The smartphone app in the intervention arm will function as described above in Aim 2, including the semi-structured interview. This intervention phase of the study will last 18 months. The NCAST feeding scale and HOME scale will be administered at visits 0, 6 months, 12 months, and 18 months. The BSID-4 will be measured at 18 months (less than an hour in duration). BSID-4 will be completed during separate assessment visits. There will be a total of 8 home visits by research staff (initial visit, 3 month follow-up visits months 1-6 and 1 visit at the end of the study for BSID-4). Also, during the home visits, research staff will also collect the following information: Infant/caregiver demographics, infant's medical history, caregiver poverty scorecard, and infant's measurements and weight. This information will be collected for research purposes only and will be obtained directly from the caregiver.

Primary Outcome:
The primary outcome is BSID-4 as a measure of infant developmental outcomes. It is a standardized assessment of cognitive, motor, and language development. Research staff interact with the child in a standardized way and observe his or her behavior.

Secondary Outcomes:
The secondary outcomes are quality of infant-caregiver interaction (NCAST feeding scale) and quality of the home environment (HOME scale). The NCAST is a standardized, reliable assessment of quality of caregiver-infant interaction. Administration consists of videotaping up to 5 minutes of the caregiver feeding the infant. The HOME is a 45-item yes/no checklist completed by an observer to measure the quality and quantity of stimulation and support available to a child in the home environment, which we have validated extensively already in rural Guatemala.

Table 2. Evidence-based guidance for infant care domains to be incorporated into smartphone application.

Care Domain	Key Guidance	Source
Sleep	* Infants sleep around 14-16 hours per day during the first 6 months * Sleep in the supine position * Sleep in the same room as the mother to support responsive breastfeeding	UNICEF - Guidance on Infant Care at Night
Feeding	* Exclusive breastfeeding for first 6 months (following WHO guidelines for acceptable medical reasons for substitute feeding) * Breastfeeding on demand (on average approximately 8-12 times/day) * Avoid additional food or drink other than breastmilk * Sleep in the same room as the mother to support responsive breastfeeding	WHO - Infant and Young Child Feeding
Activity	* Play: "Provide ways for your child to see, hear, feel, move freely, and touch you. Slowly move colourful things for your child to see and reach for. *Sample toys: shaker rattle, big ring on a string.*" * Communication: "Smile and laugh with your child. Talk to your child. Get a conversation going by copying your child's sounds or gestures."	UNICEF – Care for Child Development

Standard of Care

Aim 1 (Focus Groups) does not involve an intervention. Aims 2 and 3 will compare 2 interventions: printed caregiving materials and a smartphone application. Both interventions will be provided in addition to standard care. All subjects will be recruited from MHA clinics and will continue to be eligible for all standard of care health maintenance services in those settings, regardless of their decision to participate in the study. BSID-4 results will be discussed with the parent or legal guardian and any standard of care recommendations made.

Minimization of Risk

To protect confidentiality, the following steps will be taken:

Redcap, a secure web-based storage system for research data, will be used for all subject information except for smartphone and video data (described below). All paper research forms from research visits conducted by RAs will be kept in locked file cabinets on site in Guatemala and will be available only to research staff directly involved in this project. All research forms will have a cover sheet that codes identifying information to a unique number. This number will be transcribed to Redcap, and the cover sheet will then be removed and destroyed. Data from paper observational forms will be double-entered into Redcap, linked only to subject identifying numbers, and these will be stored separately from the key that identifies subjects. Laboratory members will have access to data identified by code for analysis and manuscript preparation, while only the PI's and the staff RA collecting it will have access to identifying information for participant tracking purposes. Once data extraction and cleaning has been completed, this key will be destroyed, and data in the analysis phase will be completely de-identified. Laptop computers used for data entry will be routinely backed-up and will be password-protected and full-disk encrypted.

For key stakeholders involved in the project, loss of confidentiality is also a concern. This is especially the case for employees of Maya Health Alliance involved in the project. To protect against this concern, the same study ID protection procedures used for children/caregivers will also be employed for the stakeholder interviews. In the monthly Implementation Team Meetings, only de-identified data from these interviews will be reviewed as relevant implementation feedback.

Smartphone Data: Our smartphone development process for this project will include end-to-end EMR integration with OpenMRS through the SanaMobile infrastructure, which integrates mHealth applications with EMRs. Both of these technologies are hosted on Maya Health Alliance secure web-based server architecture. Designing to include EMR-integration with OpenMRS will make our technology immediately applicable to numerous other global contexts where OpenMRS is in use. This platform integration also facilitates linkages between caregivers using the application and health workers, who can review incoming data and provide support to caregivers. In addition, the SanaMobile infrastructure provides a secure channel for transmission of identifiable data between end-users and clinicians. Our use of SanaMobile for collection and transmission of electronic smartphone

data will minimize risks related to privacy and security. Dr. Rohloff controls access to SanaMobile, and access will only be granted to study staff involved in the collection or analysis of smartphone data.

Video Data: video data will be stored on CHLA One Drive, a secure storage option for identifiable research data. Dr. Smith controls access to CHLA One Drive, and access will only be granted to study staff involved in the collection or analysis of video data.

Ensuring Safety of Subjects

This research meets minimal risk criteria for research with children. These intervention components involve basic interviewing, observation, and survey procedures which are unlikely to cause any degree of distress or harm to participants greater than those encountered in everyday life. No medical or invasive procedures are involved. No direct adverse events attributable to this study are anticipated, since it is a minimal risk intervention involving observation and survey procedures. The most likely adverse outcome is the potential for psychological trauma for caregivers based on assessment/interaction data with staff suggesting that their child suffers from some degree of developmental delay, which can be stigmatizing and disempowering. However, we anticipate that this risk will actually be considerably less than is the case in other existing standard of care developmental assessments and interventions, since the tool we will use here is specifically designed to be participatory and non-stigmatizing. In particular it doesn't seek to "label" children as delayed but, rather, to establish a starting point of each child on a developmental trajectory and foster progress. Nevertheless, study staff will closely track data from caregivers or staff registering dissatisfaction with or complaints about the study. PI Rohloff will review this data at least every 3 months, in order to assess whether changes to the study protocol are needed. Any potential adverse events will be reported to the Institutional Review Board. Unexpected safety concerns will also be communicated with the NIH Program Official in accordance with study regulations.

FORESEEABLE RISKS:

(Brief description of any foreseeable risks to subjects. These should include not only biomedical risks but also any and all psychosocial risks or risks related to privacy/confidentiality)

There are 5 foreseeable risks:

1. For participating infants and caregivers the primary risk is one of lost productivity or perceived interference with domestic routines and other responsibilities. Staff members may also experience a loss of productivity.
2. There is also risk of psychological stress or stigma to caregivers if protected health information is accidentally disclosed by the research team.
3. There is the risk that patients will feel compelled to participate in the research project as a condition of receiving care from MHA or to receive a good performance review if they are a staff member at MHA
4. There is the risk that there will be discordant interest between a caregiver and other family members about wanting to participate in the study which might cause conflict, particular in the case of a single mother or where other extended family members exercise significant decision making power over the primary caregiver

5. Some of the questions may make the participant feel uneasy or embarrassed. However, participants may choose to skip or stop answering questions at any time.

EXPECTED BENEFITS:
(Describe expected benefits to subjects as well as the benefit to society that may result through an increase in knowledge)

Stakeholder participants will benefit mostly indirectly from this project by helping to improve implementation knowledge around mHealth and infant development interventions in Guatemala. However, they may also benefit directly from a greater sense of empowerment and job satisfaction, by participating.

Children and caregivers enrolled in the study may benefit directly from participation. Potential benefits include improvements in developmental and growth outcomes. For caregivers, an enhanced knowledge of early child development and improved self-efficacy as caregivers are other potential benefits. Caregivers' may see improvement in some or all their child's symptoms.

The information gained through this project will contribute important, practical insights into the implementation of mHealth interventions in LMIC, at minimal risk to participants. The results of this project will develop mHealth smartphone technology which can be used to engage primary caregivers directly in the active monitoring of their infants' development, and to provide tailored feedback and support for the provision of nurturing care. In addition to design of the technology, we will also prospectively assess the implementation characteristics of the technology—usability, acceptability, and sustainability—for caregivers in a rural Guatemalan population which is at high risk for impaired infant growth and development. Following successful implementation in Guatemala, this mHealth method could then be expanded to families with at-risk infants worldwide.

EQUITABLE SELECTION OF SUBJECTS:
(No group of persons should be excluded from research, with its associated risks and benefits, without justification. Provide a justification for your selection criteria. Also, explicitly address your plan for overcoming any cultural or language barriers that pertain)

The population study sample is a convenience sample of infants and their caregivers from Tecpán, Guatemala. This population is more than 95% indigenous Maya, and many may not speak Spanish as a first language. In order to ensure equitable access to the research, the research assistants conducting visits and obtaining consent will be bilingual native speakers of Spanish and Kaqchikel Maya, the language spoken in Tecpán.

RECRUITMENT PROCEDURES:
(Provide a specific methodology that will be used for subject recruitment. Make sure to explicitly address how and by whom subjects will be approached. Also provide any details regarding efforts to enhance recruitment of minorities or women, as well as any details about remuneration)

The caregivers participating in both phases (Aim 1, design/formative phase; Aim 2, implementation/trial phase) will be recruited from among first-time caregivers receiving services at a major maternal-child wellness clinic run by Maya Health Alliance out of their main office in Tecpán Guatemala. A full time research staff member (from Maya Health alliances research core staff) will be tasked with recruitment activities. This research staff member will review planned clinical activities with maternal-child clinical team managers

on a monthly basis to ensure that they can be physically present during wellness clinic days. The research staff member will then approach caregivers in the waiting room to describe the details of the study to potential participants, including the nature of their requested involvement in the study, the possible risks and benefits of participation, and the individual capacity to withdraw from the study at any time without consequence.

We anticipate that this recruitment strategy will be successful for two reasons. First, Maya Health Alliance has successfully used this "waiting room" approach for recruitment in numerous other studies, with high success rate and meeting of recruitment targets. Second, because the research study staff conducting this recruitment will be natively fluent in both Spanish and Kaqchikel Maya, they will be able to conduct recruitment in either language, as caregivers prefer, overcoming this potential barrier to recruitment. The staff member will be able to provide details of the study and administer informed consent in either language, therefore fostering trust and improving subjects' interest in participation.

For Aim 1, up to 20 caregivers will be recruited in this fashion for formative focus groups. These participants will then be invited, as they are willing, to participate in the formative agile design phase of the app. Subsequently, in Aims 2 and 3, 40 and 220 (respectively) additional caregivers will be recruited in the same fashion into participate in the prospective implementation trial. Given cultural patterns around caregiving in Guatemala, we anticipate that most participants will be female caregivers, but we will make every effort to include male caregivers, including extending joint invitations to both caregivers, making follow-up phone calls to male caregivers when only female caregivers present to clinics, and making research home visits.

The study co-PI (Rohloff) will monitor recruitment numbers on a biweekly basis, in collaboration with the Maya Health Alliance study team, reporting to the PI Smith. If recruitment numbers are unexpectedly low, the team will consider additional strategies, such as visiting other primary care clinics in town to solicit participation of caregivers referred by other providers and distributing materials announcing the purpose of the study to civic support groups (mothers groups, church groups).

Study retention in rural Guatemala, primarily because of competing demands on time, is at times a concern. For the components of the study requiring longitudinal involvement (Aims 2 and 3), study staff will use three strategies to ensure retention: (1) collect multiple telephone contact numbers, including alternate family member contacts; (2) collect detailed information on location of subject's home, so that follow-up visits can easily be made to reestablish contact if necessary; (3) develop a formal protocol within the study operating manual, requiring multiple phone calls and at least two attempts at repeat home visits prior to considering a subject lost to follow-up. Taken together, Maya Health Alliance has used these strategies successfully in multiple other projects and are confident they will ensure a high rate of subject retention.

At each study visit, each participant will receive a small care package to compensate for their time. This will contain items commonly provided to participants in other research study and clinical nutrition encounters at Maya Health Alliance (such as high-quality food

items for family home consumption like eggs and beans, infant diapers and hygiene supplies, infant toys. Care will be taken to avoid toxic items and choking hazards). The approximate value of these items will be US $5 for each visit.

CONSENT PROCEDURES:
(Explain in detail how, where, when, and by whom consent will be obtained. Describe how coercion in the consent process will be avoided. If research involves children, make certain to fill out the supplementary form on Research involving Children)

After ascertaining initial interest in participation, a research assistant will then make a visit to the primary caregiver at their home (or in another confidential setting, as appropriate) to explain the details of the study, including the nature of the requested involvement in the study, the possible risks and benefits of participation, and the individual capacity to withdraw from the study at any time without consequence. Specific mention will be made of the fact that accessing care from MHA is not conditional on participation in the study, and that there will be no repercussions for declining to participate.

Verbal informed consent will be obtained from all participating caregivers. A verbal consent script will be read to the caregiver, and a copy of the script (in Spanish, as Kaqchikel is mostly an oral language read by very few) will also be provided. Effort will be made to obtain permission from both biological parents or legal guardians if present. However, consent from one parent/guardian will be sufficient to enroll in the trial. Assent will not be sought from enrolled children, as the participating infants (0-18 months of age) are not capable of providing assent.

In addition, given concerns that some caregivers (especially younger women or single mothers) may have restricted agency within their home and might choose to participate but have a family member countervene their decision, we will ask all caregivers if there is another individual who we should discuss the study with to get their permission and, if so, the research assistant will also explain the study to that individual and obtain their assent. In addition, for underage adolescent caregivers (<18 years), assent from the caregiver will be obtained, but consent from the adolescent's legal guardian or parent, since Guatemalan law does not recognize emancipation of minors on the basis of parenthood.

All consent procedures will occur in the language of the participant's choosing. Research staff in Guatemala will be natively fluent in Kaqchikel Maya and Spanish. Finally, research staff will have no clinical role in the care of potential subjects.

DATA SAFETY AND MONITORING:
(Describe the plan for monitoring data to ensure the safety of the subjects. This should include a description of which data will be reviewed, at what frequency, and by whom. Stopping rules should also be detailed. Describe the plan for reviewing and reporting adverse events. Consultation with an WK IRB staff member prior to filling out this section may be helpful because, based on the complexity of the protocol, an independent Data Monitoring Committee may be mandated)

No direct adverse events attributable to this study are anticipated since it is a minimal risk intervention involving observation and survey procedures. As such, no specific safety or

efficacy outcomes will be reviewed as stopping criteria.

However, the PIs will have regular meetings (biweekly) with the field team to solicit feedback on the study and identify any areas of concern that might require modification of the protocol.

MONITORING AND QUALITY ASSURANCE:
(Detail the plan to assure the validity and integrity of the data and adherence to the approved research protocol. Detail who will be responsible for this monitoring, and at what frequency.)

Study staff at Wuqu' Kawoq | Maya Health Alliance will be responsible for all initial data collection and coding. Data will be collected and uploaded to CHLA OneDrive (for video data) and MHA Redcap (for HOME score, growth data, NCAST score, BSID-4 data) applications. Both are HIPAA compliant.

The investigator team will review the rate of subject accrual, compliance with inclusion/exclusion criteria, and informed consent procedures on a monthly basis during the recruitment phase, to ensure sufficient enrollment as per the planned study protocol.

PRIVACY AND CONFIDENTIALITY:
(Detail the methods that will be used to protect the privacy of subjects and to maintain confidentiality. This should include all techniques such as deidentifying or coding data, removing health identifiers, storage and security of electronic and paper records, and the like)

To protect confidentiality, the following steps will be taken: All paper research forms from research visits conducted by RAs will be kept in locked file cabinets locally in Guatemala and will be available only to research staff directly involved in this project. All research forms will have a cover sheet that codes identifying information to a unique number. This number will be transcribed to Redcap, and the cover sheet will then be removed and destroyed. Data from paper observational forms will be double-entered into Redcap, linked only to subject identifying numbers, and these will be stored separately from the key that identifies subjects. Laboratory members will have access to data identified by code for analysis and manuscript preparation, while only the PI's and the staff RA collecting it will have access to identifying information for participant tracking purposes. One data extraction and cleaning has been completed, this key will be destroyed, and data in the analysis phase will be completely de-identified. Laptop computers used for data entry will be routinely backed-up and will be password-protected and full-disk encrypted.

DATA SHARING:
(Detail any plans to share data with collaborators outside WK, including what information will be shared and what measures will be taken to protect privacy and confidentiality)

The study involves collaborating researchers from CHLA and MHA. All identifiable data will be shared only through secure applications (OneDrive, Redcap) hosted at MHA (Redcap) or CHLA (One Drive).

Only the PIs or their delegate will have access to the study spreadsheet linking unique study

IDs to individual subjects.

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STUDY PROTOCOL

Study context and ethics oversight

This trial was conducted in collaboration with Maya Health Alliance, a primary care organization working in rural Indigenous Maya communities in Guatemala. The study was conducted in the municipality of Tecpán, Chimaltenango (population 95 000), a semi-rural community where more than 95% of the population is of Indigenous Kaqchikel Maya ancestry. The trial was conducted according to the principles in the Declaration of Helsinki, prospectively registered (NCT05106894), and approved by the Institutional Review Boards of Children's Hospital Los Angeles (CHLA-21-00168) and Maya Health Alliance (WK 2021 002).

Smartphone app design

We employed an agile design framework to develop an Android-based app. The design team included app programmers, investigators, clinical staff at Maya Health Alliance, and volunteer caregivers/end users. End users provided feedback in both focus groups and one-on-one after codesign sessions and extensive in-home usability tests. Although target participants were primarily speakers of Kaqchikel Maya the app was developed in Spanish as Kaqchikel Maya is not widely written or read. Participants who speak Kaqchikel Maya typically read and write in Spanish. App design included built-in multilingual support to permit future additions of various languages, and as many images as possible. Evidence-based caregiver recommendations in the app for breastfeeding and complementary feeding, sleep, and developmental support were selected from evidence-based sources.

Trial design and participants

This was a single-center, individually randomized (1:1 allocation ratio), parallel-group pilot trial to compare use of the smartphone app to printed educational materials. First-time primary caregivers and their infant were eligible to participate if the infant was 0-28 days old at the time of recruitment and a singleton full-term ($\geq$ 37 weeks) birth. Infant exclusion criteria were acute malnutrition (weight-for-length/height Z score ≤ -2 SD using WHO standards), severe medical illness, or medical contraindication to breastfeeding. Caregiver exclusion criteria were inability to read or speak Spanish. Eligible caregivers who did not possess a functioning Android smartphone were given a phone for the duration of the study.

Subjects were recruited by trained research nurses within usual clinical care settings after referral by healthcare providers working at Maya Health Alliance. Verbal consent was obtained following Maya Health Alliance protocol for a minimal-risk study with Indigenous populations as obtaining signatures is not a culturally common practice. Study visits and data collection occurred in the home by trained research nurses, except for the secondary outcome variable (Bayley Scales of Infant Development, Version 4; BSID4; Pearson Assessments, San Antonio, TX, USA) which was collected by consulting psychologists in clinical spaces at Maya Health Alliance.

After enrollment and randomization, caregivers received either the smartphone app, installed with assistance from a study nurse, or printed materials. Brief monthly visits (~ 15 minutes) were conducted monthly for 5 consecutive visits by a study nurse to resolve questions about the app or, in the comparator arm, to resolve any caregiver questions about the printed materials. BSID4 data was collected at enrollment and study exit at 6 months post enrollment.

STATISTICAL ANALYSIS PLAN

Quantitative statistical analysis was conducted using Stata Version 17. Demographic and clinical characteristics of study participants were summarized using means and standard deviations; median and interquartile range; or percentages, as appropriate. For BSID4 outcomes, raw differences between intervention and control arms in composite scores were summarized and adjusted differences calculated using linear regression with adjustments chosen *a priori* for sex of child, caregiver educational level, poverty score, birth weight and change in length for age Z score from 0 to 6 months.