Mobile Health Intervention to Improve Perinatal Continuum of Care in Guatemala

Protocol version date December 19, 2014

NCT02348840

Scientific protocol

Human Subjects Involvement, Characteristics, and Design.

The study will enroll participating lay midwives from the department of Chimaltenango in central Guatemala. We anticipate enrolling 50 midwives in the project. There will be no restrictions in terms of age of the enrolled participants. Participants will be required to have basic Spanish language literacy in order to enroll. Some more elderly midwives will lack the required literacy and therefore will not be eligible to enroll. However, since the project involves use of a Spanish language interface on a cellular phone, this minimum requirement is essential to program success. Additionally, in our experience, most elderly, illiterate midwives in the communities where the project will be conducted are semiretired, and most practicing midwives are literate. Therefore, we do not anticipate that a significant portion of the eligible pool of midwives will be excluded from participation based on the literacy requirement. Recruitment identification will be by word of mouth through the local site partner's well-established contacts with midwives in the community.

In addition to enrollment of midwives, who will be the primary subjects of the project, the project will also collect demographic and health data on consenting pregnant patients of each practicing midwife, as well as neonates that are born to consenting pregnant patients during the project. No data will be collected on other patient populations other than these pregnant women and their neonates. Since this is a study of the use of mHealth technology to improve pregnancy and neonatal outcomes, it is important to collect data both on the pregnant women during the pregnancy, as well as data on the neonate in the first month of life.

Of the 50 recruited midwives, 25 will be randomly assigned to receive access to the mHealth technology immediately, whereas the remaining 25 will receive the technology after 6 months. Randomization of the midwives will be performed by entering their IDs into a list and running a simple program to generate an equal number of 1's and zeros, uniquely assigned to each midwife ID. For the second half of the 12 month implementation phase, all 50 midwives will have access to the technology. This randomized "stepped wedge" design is critical to the evaluation of the project, since baseline data (for example, on referral rates to local hospitals) is not readily available. Therefore, randomizing 50% of the enrolled midwives to a delayed intervention phase will allow us to collect high quality internal baseline data that can be used to make comparisons to the early intervention arm (e.g., to compare rates of referral). At the 6 month time-point, all midwives who did not initially receive the technology will do so, which will allow all participating midwives to benefit from the training and technology by the end of the project.

In the proposed work site, midwives attend on average 10-20 births per year. This means that, over 12 months of implementation, we will have the opportunity to collect process and outcomes data on a minimum of 500 pregnant women and neonates. We will restrict enrollment of pregnant women to those who are older than 18 years of age. This is the legal age of consent in Guatemala, and this is a necessary arrangement to ensure that only consenting adults are participating in the project, as opposed to minors who are pregnant. The average age of first pregnancy in the region is 22 years of age, so the number of pregnant women who are excluded from the project due to being legal minors will be minimal. Selection of patients will be on an ad hoc basis, based on the willingness and availability of patients.

Data collection will be coordinated by field staff from Wuqu' Kawoq, the collaborating local partner. In the early intervention arm, all data will be doubly entered onto paper forms and into the mHealth/EMR interface directly by collaborating midwives. In the later intervention arm, data will initially be entered only on paper forms by midwives and then, after receipt of the technology, will also be entered into the mHealth interface. Wuqu' Kawoq field staff will collect the paper forms and check them against the EMR for accuracy. After coding into the EMR, paper forms will be destroyed.

Sources of Materials.

The research material that will be collected from human subjects will be of two forms. First, in the case of participating midwives, tests of knowledge and competence with the technology and mHealth interface will be administered by project staff. Performance data on these tests will be tabulated in an electronic spreadsheet, where each midwife will be identified by a unique identification number. A separate master sheet linking these unique numbers to each participating midwife will be maintained, accessible only by the principal investigators. At the end of the data entry and data cleaning phases, this master sheet will be destroyed. All data will be stored on a secure, HIPAA-compliant server.

Second, demographic and health outcomes data will be entered on each participating pregnant woman and resulting neonate into both paper forms and the mHealth interface. Paper forms will be collected by local field staff, checked against the EMR for accuracy, and then immediately destroyed. Each patient entered into the EMR in this way will have a unique electronic medical record number, and the project's principal investigators will maintain a list of these medical record numbers on a secure, HIPAA compliant server. Only the PI's will have access to this list. At the end of the project, this list will be used to extract the relevant outcomes data from the EMR, at which point the data will be deidentified and the master list of medical record numbers will be destroyed.

No identifiable data will be removed from the Wuqu' Kawoq servers, and will be de-identified before being downloaded to Emory University servers in the United States.

Potential Risks to Participants

The potential risks to participants from this project are minimal. For participating midwives, there is the potential risk that early randomization to the technology will create resentment among midwives who receive late randomization to the technology. To minimize this risk, all participants will receive an extensive orientation to the project design to the need to collect baseline data from half of the participants. Participants will also be reassured that all will receive equal training and access by the end of the project.

The risks to participating pregnant women and neonates are also minimal. The technologies that will be used in the project are well validated and noninvasive (Doppler ultrasound, pulse oximetry, and automated blood pressure) and routinely used worldwide in standard of care prenatal health. Therefore, no new or invasive technologies that might pose a risk to pregnancy outcomes will be employed. Furthermore, the algorithms that the mHealth interface will employ are highly conservative and designed to promote referral to physicians and to higher levels of medical care. In other words, the algorithms are designed never to "downgrade" an individual midwife's level of clinical concern and would the decision support component would never suggest against medical referral. This means

that the risk that the project would decrease health care access or falsely reassure midwives against a referral is minimal.

There is also risk of psychological stress or stigma to participating pregnant women who, for cultural or family reasons may choose to conceal the fact of their pregnancy to all but the consulting midwife. Participating in this project may contribute to inadvertent disclosure of pregnancy status to community or family members. In order to minimize this risk, project staff will limit direct interactions with enrolled pregnant women during the course of the project after obtaining consent. In other words, confidentiality and intimacy in the patient-midwife relationship will be maintained to the greatest degree possible. Project staff will interact only with the midwife and will collect relevant data only from the midwife, off-site and not within the community.

One final risk is that incorrect use of the technology may lead to a reading of an absent, excessively low or excessively high heart rate, and the relating of this information to the patient would lead to unnecessary emotional stress. Although our device is specifically designed to avoid such scenarios we will provide specific training to the midwives at the WK main site. We will follow standard training patterns, familiar to the midwives, for assembling midwives in small groups in a training room, which simulates the rural environment. The research team will provide training to the consented midwives using volunteer pregnant women. Training will be given on:

- How to interact with the consenter to allow non-coercive consent prior to any use of the study equipment or discussion of its utility.
- How to explain what they are doing during the data collection.
- How to answer questions about data use (after consent).
- How to use the device to obtain a good signal, and recognize when the signal is poor.
- How to ensure data is saved and later uploaded.
- How to label the data back to the patient in a de-identified manner if required.
- How to react to scenarios that may lead to stress on the patient such as:
 -- Finding no heart beat
 -- Heartbeat is too fast/slow
 -- Device does not work
 -- Device feels 'uncomfortable'

(In the first two cases the midwife would not reveal a problem initially to the patient, but will be trained to talk to a back-up Wuqu' Kawoq physician directly prior to disclosure).

In order to participate in the study, the midwife will have to be able to use all parts of the device correctly, and react correctly in the above scenarios. The study coordinator will assess each of the midwives for passing this test and certify that they are ready to participate. The study coordinator will also visit midwives at random in the study environment and identify deviations from the protocol requiring retaining and recertification.

Adequacy of Protection Against Risks

Recruitment and Informed Consent

Written or verbal informed consent will be obtained from all participating midwives and also from all pregnant patients of each participating midwife. There are two distinct settings and population for consenting study participants. The first group of participants is the midwives, who will be recruited and consented by the study coordinator at Wuqu' Kawoq. Midwives in Wuqu' Kawoq's catchment area will be contact by phone by the study coordinator to assess interest in the project. If a midwife expresses interest in participating they will be invited to a preliminary training session. During this training session, project staff (and in particular the study coordinator) will describe the full details of the study to potential midwife participants, including the nature of the subject's 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. The midwives will have the opportunity to ask questions about the study, after which consent to proceed will be obtained. The study coordinator will receive training in human subjects protection (e.g., CITI or the NIH module) prior to interacting with and obtaining consent with midwives.

The second group of participants that requires consenting is the pregnant mothers. All pregnant patients of each recruited midwife will be eligible for participation. Participating midwives will be encouraged to mention the study to all of their patients and to relay any potential interest in participating to the study coordinator. When a midwife identifies a pregnant subject for potentially participation, a single study staff member (a trained nurse working under the supervision of the study coordinator) will discretely visit the patient (and the biological father, if appropriate), at a location of their choosing (most likely to be the domicile of the pregnant patient) and again describe the details of the study, the risks and benefits, and the capacity to withdraw at any time without consequence, at which point verbal consent will be obtained for collection of data both during the pregnancy and in the neonatal period.

Both midwives and patients will all be bilingual speakers of Spanish and Kaqchikel Maya. Spanish is the language that they use for technical conversations, such as medical conversation. Kaqchikel is an oral, non-written language that is used in more colloquial settings. Therefore, consent (and consent documents) will be obtained in Spanish, although research staff will be able to speak both languages. We anticipate that some informal conversation and question answering will occur in Kaqchikel, after the formal consent has been read, as this is typical of medical consultations and interactions in the region: technical conversation in Spanish followed by informal clarification in Kaqchikel. In our previous experiences, we have been able to obtained written informed consent successfully, as long as attention is paid to providing clear orientation and allowing time for informal clarification and question answering. Wuqu' Kawoq's field staff all are native Spanish and Kaqchikel Maya speakers.

Protection Against Risk

Confidentiality To protect confidentiality, the following steps will be taken: All paper research forms will be kept in locked file cabinets and will be available only to research staff directly involved in this project. Immediately after checking paper forms against the mHealth/EMR interface, they will be destroyed. The EMR will be maintained on a secure, HIPAA-compliant cloud server, and only the principal investigators will have access to the EMR directly. Master lists of participating midwives and patients will be keyed to unique identifying numbers, and only the project principal investigators will have access to these

keys, which will also be maintained separately on a secure, HIPAA-compliant cloud server. One data extraction and cleaning has been completed, these master lists will be destroyed, and data in the analysis phase will be completely deidentified. Laptop computers or tablets used for data entry will be routinely backed-up and will be password-protected and encrypted.

Additional Protections for Pregnant Women, Fetuses and Neonates. This research involves the collection of demographic and health outcomes data on pregnant women and neonates. Importantly, the interventional component of the study involves an mHealth/EMR integration step and does not introduce novel or experimental technologies. All technologies that will be used in the mHealth arm are standard-of-care technologies (Doppler, blood pressure monitoring, pulse oximetry). Half of the enrolled participants will initially not receive any intervention. However, they will receive the current standard of care by lay midwives, with no interference in this usual process. Furthermore, for pregnant women and neonates who access the technology (either in the early access or later access arms), the expected result of the technology will be earlier and more timely referral to a higher level of medical care. At no point will the technology discourage accessing a higher level of care. Since the project holds out the potential for direct benefit to the pregnant woman and/or her fetus, consent will be obtained directly from the pregnant women to participate as outlined in 45cfr46 subpart B. The proposal does not include any inducements to early termination of a pregnancy, and it does not explicitly involve research on neonates of uncertain or non-viability, although in accordance with the proposal's plan to increase early access to medical care for all neonates, rates of neonatal mortality will be tracked.

Additional Protections for Children. This study involves collection of neonatal mortality rates and rates of early evaluation of neonates by a postnatal health care delivery team. As such, no direct interventions on children will be performed, and the study involves minimal risk to children. As outlined above, consent will be obtained from both biological parents at the time of enrollment of the pregnant patient in the study to permit collection of this data.

The study will not enroll pregnant patients prior to the legal age of informed consent in Guatemala (18 years).

Adverse Events. In the event that midwives either in the early technology access or later access arms detect the need for a referral to a higher level of medical care or an adverse event, they will be instructed to proceed with arranging the referral through the usual local mechanisms. However, the local site partner, Wuqu' Kawoq, will also designate a medical officer to assist with the project, and this physician will be available to all midwives throughout the duration of the project to provide further logistical and decision support for arranging referrals and management of adverse events.

Potential Benefits to Study Participants

Participants are likely to benefit directly from this project. Midwives will benefit by gaining access to additional medical knowledge and technology. Pregnant women and neonates will benefit by earlier detection of the need for medical referral and improved care coordination. The risk of the project are minimal, and the potential benefits of the project, which include the demonstration that mHealth technology can be used to enhance the care provided by lay midwives in a developing country setting where perinatal outcomes and care coordination are generally poor outweigh these risks.

Importance of the Knowledge to Be Gained

The information gained through this project will contribute important, practical insights into the implementation of a mHealth solution to low rates of medical referral and care coordination for pregnant women and neonates. These are perennial public health problems in rural Guatemala which have until now proven to be largely intractable. In addition to suggesting new avenues for enhancing care in rural Guatemala, the results will also be applicable to other rural populations in other developing countries which experience similar breaks in the primary care referral chain and the continuum of care.

Institutional Review Board Coverage

The project will be supervised by the IRB of Emory University. In addition, the study will also be reviewed and approved by the IRB of the local implementing partner, Wuqu' Kawoq. Both of these institutions have OHRP approved IRBs with FWA. All field staff participating in the project will approve an on-line course on the protection of human subjects participating in research.

Inclusion of Women and Minorities

Study participants will include 50 lay midwives from the department of Chimaltenango in rural Guatemala. Midwives in rural Guatemala are all female for cultural reasons. All participants will likely be of Maya ethnicity. Although there will be no restrictions in terms of ethnicity for enrolment, the area in which the study is taking place is composed almost exclusively of ethnic Maya speaking the Kaqchikel language. Indeed, the purpose of the study is to explore ways to improve maternal and child outcomes in this population, which experiences wide disparities in health care access and outcomes when compared to other inhabitants of Guatemala who are not ethnically Maya and live in other parts of the country. See Targeted/Planned Enrollment Table for projected target sizes of subgroups based on gender and race/ethnicity.

Inclusion of Children

Because of the stigma associated with teenage pregnancy, and our desire to involve any elevated risk of stigma by inadvertently identifying teenage pregnancies against their will, only pregnant woman above the age of legal consent in Guatemala (18 years) will be included in the project.

Neonates who are born to consenting parents during the project, and data on neonatal referrals and mortality will be collected from the electronic medical record. No neonates born to consenting parents will be excluded from this data collection.

FDA submission

Results from this project will no be sent to the FDA.

Targeted/Planned Enrollment Table shows projected target sizes of subgroups based on gender and race/ethnicity.

Study Title: **Mobile Health Intervention to Improve Perinatal Continuum of Care**

Total Planned Enrollment: **1050**

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males(*)**	**Total**
Hispanic or Latino	800	250	1050
Not Hispanic or Latino	0	0	0
Ethnic Category: Total of All Subjects *	800	250	1050
Racial Categories			
American Indian/Alaska Native	800	250	1050
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
Racial Categories: Total of All Subjects *	800	250	1050

* The “Ethnic Category: Total of All Subjects” must be equal to the “Racial Categories: Total of All Subjects.” ** Any children born in the study are considered part of the enrollment. With 500 anticipated births, 50% of these are anticipated to be male