

Evaluation of a Two-Way SMS mHealth Strategy to Reduce Neonatal Mortality: Rationale, Design and Methods of a Randomized Controlled Trial in Kenya

Keshet Ronen (✉ keshet@uw.edu)

University of Washington <https://orcid.org/0000-0001-5625-4884>

Esther M Choo

University of Washington

Brenda Wandika

Kenyatta National Hospital

Jenna Udren

University of Washington

Lusi Osborn

Kenyatta National Hospital

Peninah Kinthao

Kenyatta National Hospital

Anna Hedstrom

University of Washington

Millicent Masinde

Kenyatta National Hospital

Manasi Kumar

University of Nairobi

Dalton Wamalwa

University of Nairobi

Barbra A Richardson

University of Washington

John Kinuthia

Kenyatta National Hospital

Jennifer A Unger

University of Washington

Study protocol

Keywords: mhealth, SMS, neonate, mortality, depression, Kenya

Posted Date: April 1st, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-371505/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Globally, approximately half of the estimated 6.3 million under-5 deaths occur in the neonatal period (within the first 28 days of life) and 75% of neonatal deaths occur in the first week of life. Kenya ranks among countries with the highest number of neonatal deaths, with a neonatal mortality rate of 20 per 1000 live births. Novel strategies are needed to meet the WHO's Every Newborn Action Plan target of 10 or fewer neonatal deaths per 1000 live births by 2035. Improved identification and management of neonates with potentially life-threatening illness is critical. We developed an interactive (two-way) human-computer hybrid SMS intervention, Mobile Solutions for Neonatal Health (Mobile WACH NEO), focused on the perinatal period when risk to mothers and infants is highest. Mobile WACH NEO sends automated tailored and personalized SMS messages to mothers during pregnancy and up to 6 weeks postpartum. Messages employ the Information-Motivation-Behavior Skills (IMB) behavioral theory framework to promote 1) maternal implementation of essential newborn care (ENC, which includes early breastfeeding, exclusive breastfeeding, cord care and thermal care), 2) maternal identification of neonatal danger signs and care-seeking, and 3) maternal social support and self-efficacy. Participants can also send SMS to the study nurse, enabling on-demand remote support.

Methods: We describe a two-arm unblinded randomized controlled trial (RCT) of the Mobile WACH NEO SMS intervention. The RCT will enroll 5000 third trimester pregnant women in 4 facilities in Kenya and randomize them 1:1 to receive interactive SMS communication or no SMS (control), and conduct follow-up study visits at 2 and 6 weeks postpartum. Neonatal mortality will be compared between arms as the primary outcome. Secondary outcomes include care-seeking, practice of ENC, and psychosocial health. Exploratory analysis will investigate associations between maternal mental health, practice of ENC, care-seeking and SMS engagement.

Discussion: This study will contribute evidence on the impact of two-way SMS in a low-income setting on neonatal outcomes, using a rigorous evaluation design. This study will build evidence to fill a gap in understanding drivers of neonatal outcomes and the potential impact of SMS interventions.

Trial registration

Trial registration: clinicaltrials.gov, NCT04598165. Registered October 22, 2020 – retrospectively registered. <https://clinicaltrials.gov/ct2/show/NCT04598165>.

Introduction

Background and rationale {6a}

Half of all deaths under the age of 5 occur in the neonatal period, defined as the first 28 days of life, and 75% of these neonatal deaths occur during the first 7 days of life.¹ The proportion of under-five mortality that occurs in the neonatal period increased from 40% in 1990 to 47% in 2018.² In Kenya, the neonatal mortality of 20 per 1000 births remains higher than the global average of 18 per 1000 births, and among

women living in poverty and rural areas, the rates are substantially higher.^{2,3} Novel strategies are needed to prevent these deaths and attain Sustainable Development Goal (SDG) 3.2.2 of reducing global neonatal mortality to less than 12 per 1,000 live births by 2030.⁴

The World Health Organization (WHO) Every Newborn Action Plan (ENAP) identifies priority strategies to reduce neonatal mortality, including practice of essential newborn care (ENC), prompt identification and care-seeking for newborn danger signs, and preventative treatments including vaccinations.^{1,5,6} ENC practices of early and exclusive breastfeeding, clean cord care, and thermal care have been independently shown to reduce neonatal death.^{7–10} For low birthweight and premature newborns, kangaroo mother care (KMC) support is recommended in addition to ENC.⁵ While provision of ENC can prevent neonatal illness, decisions about care-seeking when neonatal illness occurs are also key to neonatal survival.

Although ENC and appropriate care seeking interventions show high efficacy, in general, adoption of these practices remains low, particularly in places with high neonatal mortality. Studies in Ethiopia, Uganda, Ghana, Malawi, Mali, and Tanzania show sub-optimal practice of ENC with a range of 28–92% of caregivers applying inappropriate substances to the cord, over 50% of newborns bathed within 6 hours post-delivery, and less than 50% of newborns initiating breastfeeding within the first hour in half of the countries in sub-Saharan Africa.¹¹ Similarly, delays in recognizing illness and deciding to seek care contribute up to 80% of neonatal and child deaths.^{12–15} The three delays model posits that neonatal deaths are due to delays in (1) identifying illness and deciding to seek care, (2) reaching the health facility, and (3) receiving quality care once a facility is reached.¹⁶

Reasons for lack of ENC adoption and delayed care-seeking are complex, but it is thought that some can be overcome by supporting caregivers, typically mothers, to provide ENC, to identify neonatal illness when it occurs, and to seek timely facility-based care. From an individual perspective, a mother's mental health, sense of self-efficacy, socioeconomic status and social support network influence her ability and decision to practice ENC and seek care. Maternal depression has been associated with lower care-seeking and preventive practices for infants,¹⁷ as well as adverse infant outcomes including premature delivery,^{18,19} low birth weight,²⁰ decreased initiation of breastfeeding,¹⁸ perinatal death,²¹ delays in cognitive development,^{22–24} infant illness,²⁵ poor infant social engagement,²⁶ and poor safe child practices.²⁷ Social support is thought to be a mediator in the relationship between depression and low birth weight, suggesting that higher social capital helps to improve birth outcomes.^{28,29} Parental self-efficacy, the belief caregivers have the ability to effectively care for their newborns, is also associated with positive parenting,³⁰ as well as greater initiation and longer duration of breastfeeding.³¹ Conversely, a caregiver with low self-efficacy may delay seeking care due to lack of confidence in making healthcare decisions, leading to poor neonatal outcomes. Among other factors, regular close contact with those in a caregiver's social support network during the early postnatal period is a major predictor of parental self-efficacy.^{32–34} Thus, improving the domains of maternal mental health, self-efficacy and social support may result in better neonatal outcomes.

Mobile health (mHealth) interventions offer innovative approaches to promote ENC, reduce the delay in identification of newborn illness at home, improve timely care-seeking, and provide maternal psychosocial support during the neonatal period. In Kenya, where 89% of the population own mobile phones,^{35,36} the Ministry of Health has embraced mHealth interventions.³⁷ Interactive (two-way) short messaging services (SMS) between mothers and healthcare workers (HCW) holds promise to connect the poorest and most remote communities with timely and appropriate health information targeted to reduce neonatal and maternal adverse outcomes.³⁸ These technologies have been used to deliver health information, reinforce self-efficacy, address depressive symptoms, facilitate visit reminders, and increase communication between HCWs and patients, all with a goal of improved maternal-child health.^{39–46} However, no previous studies have rigorously evaluated the impact of two-way SMS on neonatal outcomes.^{39,47–49}

This protocol outlines a multi-site individually randomized controlled trial (RCT) to test the impact of a novel two-way SMS intervention on neonatal mortality, practice of essential newborn care actions, and mothers' psychosocial health in Kenya. Grounded in the Information-Motivation-Behavioral Skills (IMB) model of behavioral change,⁵⁰ we hypothesize that the SMS intervention will reduce neonatal mortality through the mechanism of improved identification of neonatal illness, information, and skills for ENC provision and care-seeking, as well as improved motivation through increased social support, increased self-efficacy, and reduced perinatal depression.

Objectives {7}

Our objectives are to: (1) determine the effect of Mobile WACH NEO on neonatal mortality, (2) determine the effect of Mobile WACH NEO on maternal implementation of essential newborn care and care-seeking behavior, and (3) determine the effects of Mobile WACH NEO on maternal social support, self-efficacy and depression.

Trial design {8}

The Mobile WACH NEO study is a multi-site, two-arm, 1:1 individually randomized, parallel group, superiority RCT comparing peripartum interactive two-way SMS to standard of care (no SMS) control. The aim of the study is to determine the impact of Mobile WACH NEO interactive SMS on neonatal mortality, care-seeking for infant illness, practice of ENC, and maternal mental health. Post-RCT qualitative in-depth interviews among intervention arm participants aim to characterize determinants of SMS engagement and to evaluate participants' experiences with the intervention.

Methods: Participants, Interventions And Outcomes

Study setting {9}

The study is conducted at four healthcare facilities in Kenya: Mathare North Health Centre, Riruta Health Centre, Rachuonyo County Hospital and Bondo Sub-County Referral Hospital. Two facilities (Rachuonyo and Bondo) are in rural locations in Western Kenya, and two facilities (Mathare and Riruta) are in urban locations in Nairobi. These sites were chosen to include Nairobi, Homa Bay and Siaya counties, which all have high neonatal mortality.³

Eligibility criteria {10}

Women are eligible to participate if they are ≥ 14 years old, pregnant at 28-36 weeks estimated gestational age, enrolled in antenatal care at a study site, have daily access to a shared or personal mobile phone with a subscriber identity module (SIM) on the Safaricom network, are willing to receive SMS, plan to stay in the area for 5 months or greater, and are not enrolled in another study. Literacy is not required if a woman has access to a partner or trusted person who she is comfortable having read her the messages. The approach of involving partners in receiving and sending SMS was developed in consultation with Kenyan mothers and successfully implemented in prior Mobile WACH studies.^{51,52}

Who will take informed consent? {26a}

Potential participants are identified in antenatal clinics by clinic staff, informed about the study, and referred to study nurses for eligibility screening. Study staff obtain verbal consent from potential study participants prior to eligibility screening. If a woman is eligible for trial participation, study staff undertake the process of informed consent and obtain written consent. When potential participants are illiterate, an impartial witness is present during the entire consent process and signs the consent form. The age of consent in Kenya is 18, but pregnant women age 14 or older are considered emancipated and can consent independently, thus all eligible study participants are able to consent independently.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

Consent includes permission to conduct home visits or phone interviews for tracing purposes and to conduct a verbal autopsy in case of an infant death. The consent also includes permission to use de-identified participant data in future studies. Biological specimens are not collected in this RCT.

Interventions

Explanation for the choice of comparators {6b}

Inclusion of a control arm isolates the effect of Mobile WACH NEO on primary and secondary outcomes. All participants receive current standard of care and education provided in antenatal care (ANC) and postnatal care (PNC) by MCH clinic staff. Women randomized to the control arm do not receive SMS messages from Mobile WACH NEO. Interaction with study personnel only occurs for study data collection during follow up visits.

Intervention description {11a}

Participants randomized to the two-way SMS arm receive a series of automated SMS messages during pregnancy and until 6 weeks postpartum. Message content is designed based on estimated gestational age or time since delivery. Messages are sent in English, Dholuo or Kiswahili depending on the participant's preference. Participants can send SMS messages to the study at any time and study nurses respond by SMS during business hours within one business day through a web-based platform. Sending and receiving SMS is at no cost to the participant.

SMS messaging content during the pregnancy and postpartum periods are summarized in Figure 2. From enrollment up to 38 weeks gestation, automated SMS are delivered weekly, encouraging facility delivery and birth planning, and providing anticipatory information about neonatal danger signs and emotional support. Automated SMS are delivered at a pre-specified day, time and language based on participant preferences. From 38 weeks gestation until delivery, women receive daily messages highlighting identification of neonatal danger signs and ENC practices including immediate and exclusive breastfeeding, thermal and cord care. From delivery to 2 weeks postpartum, mothers receive two messages per day: one message with screening questions for identification of infant danger signs and encouragement to engage with nurses by SMS if they have a concern, and one message with educational content on ENC practices, mental health and support. From 2 to 6 weeks postpartum, SMS are delivered every other day. All messages are personalized with the participant's preferred name and contain a prompt to engage women in message content. Participants in both the control and intervention arms receive standard ANC and MCH clinical services through MOH clinics with minimal in-person interactions with study personnel.

Messages were adapted from prior Mobile WACH studies,^{51–53} consistent with Kenyan Ministry of Health guidelines for newborn care,⁵⁴ and tested during a pilot study involving 800 peripartum women in Mathare North Health Center and Rachuonyo County Hospital.⁴⁶ The messaging curriculum was modified through consultations with obstetrics, neonatology, and mental health specialists and literature review on supportive messaging. Messages are personalized by opening with the participant's name. They are action-oriented and address a specific outcome of the trial. Additional messaging “tracks” were created with adaptations to the messages for mother-infant dyads at elevated risk for obstetrical and neonatal complications. Those placed in high-risk tracks receive additional messages tailored to their specific risk factor. High-risk groups include (1) first-time mothers or mothers age ≤ 19 , (2) women who screen positive for elevated depression symptoms during study data collection using the Edinburgh Postnatal Depression Scale (score ≥ 13) or (3) women whose infants are born premature (< 37 weeks estimated gestational age) or are of low birth weight (< 2.5 kg). Additionally, if a participant loses her pregnancy or her infant dies and she consents to continued messaging, she is switched to a message track that contains no content related to pregnancy or infant care but includes emotionally supportive condolence messages designed in a previous Mobile WACH study.⁵⁵ Messages sent to participants in specific tracks attempt to capture a broad group at higher risk of poor pregnancy or neonatal outcomes who may benefit from targeted messaging.

The Mobile WACH NEO SMS curriculum was developed based on the IMB theory, which holds that health behavior is influenced by an individual’s knowledge of information about the benefits of the behavior, their motivation to change behavior, and their skills to change and engage in new behavior (Figure 1).⁵⁰ Based on this model, topics and example messages sent in the study are summarized in Table 1.

Table 1: Example Mobile WACH NEO SMS Based on IMB theory

Construct	Day	Example messages
Information		
• Care seeking	1 week before estimated due date	{name}, this is {nurse} from {clinic}. Did you know that newborns should be taken to the health facility if they stop breastfeeding well, develop a fever, are breathing fast or become less active? How will you get to your nearest health facility in case of an emergency?
• Delayed bathing / thermal care	Day of delivery	{name}, this is {nurse} from {clinic}. Newborns need to be kept warm. The baby is wiped right after birth. Keep the baby bare skin-to-skin with you and cover you both. Dress the baby in socks, a nappy and hat. Place the baby on your naked chest and cover both of you. This contact helps with bonding, breastfeeding and keeps the baby warm. It is very important to avoid bathing your baby in the first two days. Do you have questions about keeping your baby warm or the bath?
• Initiation or exclusive breastfeeding	2 days postpartum	{name}, this is {nurse} from {clinic}. Your milk should start to “come in” between birth and day 5. Breastfeed your baby often, don’t skip breastfeedings (even at night), ensure good attachment/positioning, and let baby finish the first breast before offering the other side. To decrease discomfort from swollen breasts, use cold and/or cabbage leaf compresses between feedings. If baby is having trouble attaching to the breast properly during breastfeeding due to swollen breast, express milk from the swollen breast until the nipple is soft, then try putting the baby on the breast again.
• Newborn practices to prevent infection	3 days postpartum	{name}, this is {nurse} from {clinic}. Once the baby is born you can prevent infections by washing your hands and keeping the cord clean. Do not apply any substances or bandages to the cord. Do you have any questions about taking care of the baby’s umbilical cord?
• Kangaroo Mother Care for low birthweight/ preterm	4 days postpartum	{name}, this is {nurse} from {clinic}. Hold your baby skin-to-skin as much as possible throughout the day. This will help them grow. How is skin-to-skin holding/kangaroo care going for you and your baby? Also be sure to monitor the baby’s umbilical cord. Do not apply any substance or bandages to it but let us know if it is red or there is discharge.
• Identification of neonatal danger signs	4 days postpartum	{name}, this is {nurse} from {clinic}. Is the baby having any trouble breathing? Do they seem very hot or cold? These are danger signs and could mean the baby is sick. Please let us know right away.
Motivation		
• Depression	10 weeks and 5 days before expected delivery date	{name}, this is {nurse} from {clinic}. Sometimes pregnancy and motherhood can bring on sadness, anxiety or worry. This happens to many women and can cause you to feel alone, cry and have difficulty sleeping. Are you having any of these problems?
• Social support	24 days postpartum	{name}, this is {nurse} from {clinic}. How are you and the little one doing today? We know it is a new experience and some days are much difficult than others. You and the baby are learning and growing everyday. You are doing a good job and we are here to help with any advice you might need. Please SMS us with any concerns.

• Self-Efficacy	28 days postpartum	{name}, this is {nurse} from {clinic}. How are you doing today? We know you are doing your best and we want to thank you for all the good work you put into supporting your little one. Make sure you take a few minutes to appreciate your hard work and let us know if there are areas where you are experiencing difficulties such as feeding the baby, experiencing problems in sleeping or feeding, difficulties looking after or connecting with the baby, anxious or sad feelings coming up. We are here to help. Which of these difficulties are you having?
Behavioral Skills		
• Instrumental support	13 and 6 days before estimated delivery date	(name), this is (nurse) from (clinic). Regular, strong stomach pains are a sign of labour. If you feel this strong tightening regularly pains, leaking of fluid or bleeding, go to the facility. Do you feel any contractions? Do you have any concerns?
• COVID-19	4 days before estimated delivery date	{name}, this is {nurse} from {clinic}. Even during this time of the COVID-19 epidemic, you still need to go to the clinic. Only stay at home if you are having symptoms of the Coronavirus like cough or fever. Coming to the clinic, including at delivery, is still very important for you and the baby. Do you have any questions or concerns about the COVID-19 virus?
• Interactive triage	14 days postpartum	{name}, this is {nurse} from {clinic}. By two weeks old a newborn baby may cry up to 2 hours a day. Make sure your baby is not hungry, tired or has a dirty diaper/nappy. Pay attention to what calms your baby like singing, rocking, swaddling or sucking. Does your baby cry for more than 30 minutes at a time? Please let us know when you are having any problems with your baby.
• Instrumental support	16 days postpartum	{name}, this is {nurse} from {clinic}. Getting to know your newborn and their schedule can be hard especially when you are not getting enough sleep. It is normal to feel tired and to need help. Do you have someone to help you or have concerns that maybe the nurse can help with?

A custom human-computer hybrid software system is used to manage incoming and outgoing SMS for Mobile WACH NEO (Figure 3).^{52,56} This system enables seamless two-way SMS communication and participant tracking. To facilitate management of messages, the messaging platform was developed through a human-centered design processes with Kenyan nurses to improve usability and streamline workflow.⁵⁶ The interface enables nurses to review incoming participant SMS and counsel on potential medical conditions or concerns within one business day. The system also has a bank of responses to frequently asked questions, such as common pregnancy concerns, birth planning, infant feeding, and infant illness, which nurses can use as a modifiable template for their responses. This allows for improved standardization and response times. Nurses also can freely respond to participant messages or questions that arise. Nurses triage messages as they are received and respond with greater urgency to messages involving a reported maternal or neonatal danger sign, serious adverse event, or home delivery. If participants report neonatal or maternal danger signs, they are referred to facility care by study nurses. If a participant reports experiencing intimate partner violence, suicidal ideation, elevated depressive

symptoms, or severe food insecurity, study staff refer the participant to available local resources. Prior to study initiation, study personnel received training on use of the SMS system and topics in neonatal, maternal health and psychosocial support. Study messages are reviewed weekly by senior team members and discussed with study nurses for quality assurance.

Criteria for discontinuing or modifying allocated interventions {11b}

Participants enrolled in the intervention arm can opt out of the intervention at any time or send an SMS to withdraw from the intervention. If a participant reports a pregnancy or infant loss, they automatically stop receiving automated messages and are offered the option to continue receiving modified messages, as described above. To comply with movement restrictions during the COVID-19 pandemic, home-tracing is not conducted.

Strategies to improve adherence to interventions {11c}

All SMS messages include a question to the participant to encourage interaction with study nurses. To ensure timely transition from antepartum to postpartum messaging at delivery, participants are encouraged to report their delivery as soon as possible by SMS or phone call. Participants without a recorded delivery by 1 week after their estimated delivery date are contacted by phone call to confirm their delivery status. If they are not reached by phone tracing, home tracing is performed. If delivery is not confirmed by 43 weeks gestational age and tracing is unsuccessful, the participant automatically starts receiving postpartum messaging.

Relevant concomitant care permitted or prohibited during the trial {11d}

Study participants receive all routine clinical care at the facility. All participants who are identified as experiencing intimate partner violence, suicidal ideation, elevated depressive symptoms, or severe food insecurity are referred to available resources and additional assistance regardless of study arm.

Provisions for post-trial care {30}

No provisions for post-trial care are offered to participants.

Outcomes {12}

The primary outcome of the study is neonatal death, defined as death within the first 28 days after live birth. All study outcomes are outlined in Table 2.

Table 2: Mobile WACH NEO study outcomes

Description	Indicator	Timing of ascertainment	Analysis metric	Statistical method
Primary outcome				
Neonatal mortality	Death during 1 st 28 days of life	2-and 6-week visits, record abstraction	Comparison of proportions	Log-binomial regression
Secondary outcomes				
Early neonatal mortality	Death during 1 st 7 days of life	2-and 6-week visits, record abstraction	Comparison of proportions	Log-binomial regression
Initiation of early breastfeeding	Breastfeeding in 1 st hour of life	2-week visit	Comparison of proportions	Log-binomial regression
Exclusive breastfeeding	Cessation of exclusive breastfeeding in 1 st 6 weeks of life	2-and 6-week visits	Comparison of time to event	Cox proportional hazards
Thermal care	Bath in 1 st 24 hours of life	2-week visit	Comparison of proportions	Log-binomial regression
Cord care	No application of substances to cord	2-week visit	Comparison of proportions	Log-binomial regression
Home provision of Kangaroo Mother Care	Any duration skin-to-skin care on ≥ 10 of the first 14 days at home, among low birthweight or preterm infants	2-and 6-week visits	Comparison of proportions	Log-binomial regression
Maternal knowledge of neonatal danger signs	Number of the 7 danger signs or symptoms successfully named	2-and 6-week visits	Comparison of means	Poisson GEE
Appropriate care seeking	Number of clinic visits with danger sign and/or hospital admissions reported in 1 st 6 weeks	2-and 6-week visits	Comparison of means	Poisson regression
Elevated depressive symptoms	Score above ≥ 13 on Edinburgh Postnatal Depression Score	Enrollment, 2-and 6-week visits	Comparison of proportions	Log-binomial GEE
Social support	Score using MOS Social Support Survey	Enrollment, 2-and 6-week visits	Comparison of means	Linear GEE
Self-efficacy	Score using Karitane Parenting Confidence Scale	Enrollment, 2-and 6-week visits	Comparison of means	Linear GEE

Participant timeline {13}

The participant timeline is depicted in Figure 4. Participants enter the study at 28-36 weeks gestation and are randomized to either the Mobile WACH NEO or control arm at enrollment. At 2 and 6 weeks following delivery, participants attend a study visit in conjunction with their usual medical care at the clinic or complete a study visit by phone, in which study nurses verbally administer a questionnaire to ascertain delivery information and data on primary and secondary outcomes. Following the 6-week study visit, in-depth interviews are conducted with 60 intervention participants to gather data on their experience with the SMS curriculum. In addition, verbal autopsies are conducted via phone or in person 6 weeks or more after an infant death occurs. Participants are enrolled in the study until 18 weeks after delivery to allow time for all follow-up activities, including in-depth interviews and verbal autopsies as needed.

Sample size {14}

The study is powered to detect a difference in the primary outcome of neonatal mortality. With 5,000 participants randomized 1:1 to SMS and control, assuming 10% attrition and $\alpha=0.05$, we have 80% power to detect a hazard ratio of 0.53 assuming a neonatal mortality rate of 23 per 1000 in the control arm. With this sample size, assuming $\alpha=0.0045$ (Bonferroni-adjusted for 11 tests, see data analysis section below), we will also have 80% power to detect the following changes in secondary outcomes: a risk ratio of 1.05 in early initiation of breastfeeding assuming 80% uptake in controls, a risk ratio of 1.11 in application of substances to the cord or delaying first bath assuming 50% in controls, a risk ratio of 0.76 in elevated depression symptoms assuming 19% in controls.

Sample size for post-RCT qualitative data collection was determined based on the number of interviews needed to achieve saturation of concepts. It is estimated that 60 interviews will be sufficient to achieve saturation and provide relevant intervention and implementation feedback.

Recruitment {15}

Study staff obtain a list of women presenting for ANC visits at the clinic each day. They then approach potential participants at ANC visits and provide a short description of the study. If a potential participant is interested in learning more about the study, study staff perform eligibility screening following the antenatal care visit.

Assignment of interventions: allocation

Sequence generation {16a} and Concealment mechanism {16b}

Enrolled pregnant women are randomized to two-way SMS or control, using 1:1 allocation (Figure 4). A web-based randomization service generates allocations, stratified by site, using random block sizes of 2, 4, and 6 (Randomize.net, Ottawa, Canada). The randomization service only displays and records the allocation after staff have entered the enrolled participant ID. The study arm is unblinded to participants

and study staff. To ensure participants are distributed across sites, no site will enroll more than 2499 of the 5000 total women. In rare situations where randomization using the web-based service is not possible due to technical issues, envelopes containing randomization allocations generated by the web-based service are available.

Implementation {16c}

The allocation sequence is generated by the web-based randomization service and is not available to investigators or staff in advance of randomization. Study staff at each of the four sites enroll and assign participants to the arms from the randomization allocations obtained through the web-based randomization service.

Assignment of interventions: Blinding

Who will be blinded {17a}

Participants and study staff are not blinded. The principal investigator and co-investigators are blinded to study findings until study close.

Procedure for unblinding if needed {17b}

There is no provision for unblinding as both participants and study staff are unblinded in this trial.

Data collection and management

Plans for assessment and collection of outcomes {18a}

Data are collected at study visits at enrollment in pregnancy, 2 weeks postpartum, and 6 weeks postpartum. At enrollment, a tablet-based enrollment questionnaire using an open-source tablet-based data collection system (KoboToolbox) is used to collect data on demographics, clinical and pregnancy history, family planning, experience with SMS and technology, social support, intimate partner violence, maternal and child health status, breastfeeding plans, parental self-efficacy, and depression. To determine estimated delivery date (EDD) at enrollment, women are asked the date of the first day of their last menstrual period. EDD is also abstracted from the MCH booklet, the primary medical record used in the peripartum period, when available. In cases of disagreement between LMP and EDD, the MCH booklet is the primary data source. Dates for follow-up visits are calculated based on actual delivery date once delivery has occurred.

At 2-week and 6-week follow-up visits, a standardized questionnaire is administered using KoboToolbox to capture infant mortality, knowledge of essential newborn care practices, neonatal danger signs, appropriate care seeking for any instances of infant or maternal illness that have occurred since delivery, peripartum depression, social support, and parenting self-efficacy. The 2-week follow-up visit questionnaire additionally captures details on immediate breastfeeding, delivery, thermal and cord care. Study visits are designed to align with routine patient clinical care schedules. In response to the COVID-19

pandemic, the research team modified study procedures to suspend any in-person home visits or clinic visits only for data collection procedures. Follow-up data collection occurs via in-person study visits aligned with routine clinical care or via phone, following Ministry of Health guidelines and recommendations to reduce possible exposures to COVID-19. The study also complements data collection at study visits with abstraction of clinic record data about hospitalizations and deliveries. The primary source of abstracted data for maternal or infant hospitalization is the hospital discharge form brought by the mother to the 2- or 6-week study visits. Medical record abstraction is also performed to collect delivery details if a participant misses the 2- or 6-week study visit(s). The primary source of abstracted data on delivery is the MCH booklet brought by the mother and the maternity registry at the clinic. Abstracted data are entered into an electronic data collection system using REDCap.

When the study is informed of an infant death, a verbal autopsy is conducted to determine the primary causes of death, using the Population Health Metrics Research Consortium (PHMRC) shortened verbal autopsy neonatal questionnaire.⁵⁷ The primary cause(s) of death are generated using the SmartVA – Analyze 2.0.0 application.

To ensure data quality, questionnaires at each study visit contain programmed range checks for plausible data values and automatic skip patterns. Data checks are performed on a weekly basis to identify data errors.

Plans to promote participant retention and complete follow-up {18b}

Active tracing by phone is conducted if a study participant misses a 2- or 6-week study visit by 1 week or no delivery date is recorded by 1 week after EDD. If the participant is not reached by phone after four attempts, home tracing is conducted. Participants who do not wish to come to clinic for the 2- or 6-week study visit are offered to complete the questionnaire by phone or at home if suitable locations for ensuring participant confidentiality are available. To comply with movement restrictions during the COVID-19 pandemic, the follow-up visits, verbal autopsy and in-depth interviews are offered via phone and home-tracing is not conducted.

Data management {19}

Data are collected digitally and uploaded daily to a secure cloud storage location accessible only by key data management personnel. Access to electronic data capture systems used in this study, including KoboToolbox and REDCap, is limited to study staff who conduct data entry and management. Data systems, including the SMS platform, are password protected and accessible only by authorized users. The data manager generates weekly reports for study monitoring and to identify errors in data. Resolution of data errors is documented thoroughly in data management logs and during data cleaning.

Confidentiality {27}

Any personally identifiable information related to participants is maintained separately from study data to preserve participant confidentiality. Paper forms such as signed consent forms are stored in locked cabinets separate from forms connecting participant names and their study participant identifier. All participants are assigned a study identification number (ID) and identified only by that ID after enrollment. Discussions between study staff and potential participants during study visits or for purposes of data collection are conducted in a private space to maintain privacy.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

There are no plans for collection of biological specimens.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

Study outcomes and analytic approaches are summarized in Table 2. The primary study outcome is neonatal mortality, defined as death within the first 28 days of life as reported in clinic records or maternal report. Risk of neonatal mortality will be compared between arms by log-binomial regression. Secondary outcomes are: neonatal mortality in the first 7 days (analyzed by log-binomial regression), proportion of mothers who initiate exclusive breastfeeding in the first hour of life (analyzed by log-binomial regression); proportion of mothers who delay bathing for at least 24 hours after birth (analyzed by log-binomial regression); proportion of mothers who apply no substances to the umbilical cord (analyzed by log-binomial regression); time to cessation of breastfeeding (analyzed by Cox proportional hazards regression); proportion of mothers of preterm or low birthweight neonates who provide kangaroo mother care (analyzed by log-binomial regression); number of neonatal danger signs successfully named by the mother (analyzed by generalized estimating equation Poisson regression); proportion of women with elevated depression symptoms by Edinburgh postnatal depression scale (analyzed by generalized estimating equation log-binomial regression); social support score by the MOS Social Support Scale (analyzed by generalized estimating equation linear regression); self-efficacy score in the Karitane Parenting Confidence Scale (analyzed by generalized estimating equation linear regression).

All analyses will be intent-to-treat. Analysis of secondary outcomes will be corrected for multiple comparisons using the Benjamini-Hochberg method.⁵⁸ Power calculations were conducted using a Bonferroni adjustment to provide a conservative estimate of the limits of detectable differences.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

Primary analysis will be intent-to-treat, but an exploratory per-protocol analysis will be conducted excluding women who discontinue the SMS intervention. Based on previous studies in this population, we expect 10% loss to follow-up between enrollment and the 6-week study visit. Sensitivity analyses will be

conducted for the primary mortality outcome assuming all participants who are lost to follow-up and missing mortality data did or did not experience neonatal mortality.

Interim analyses {21b}

An interim analysis for neonatal mortality will be performed using O'Brien-Fleming boundaries for benefit and harm when 50% of expected person time has been accrued.

Methods for additional analyses (e.g. subgroup analyses) {20b}

Participants from the intervention arm will be purposively sampled to participate in IDIs based on their engagement in the Mobile WACH NEO intervention. Participants will be divided into high, medium and low interactor groups based on messaging behavior collected on the Mobile WACH system. From each group, ten participants will be randomly selected to complete interviews. These interviews will focus on barriers and facilitators of SMS engagement to characterize high and low users. In addition, we will interview thirty women whose neonates had complications or died to understand perceived utility of remote engagement with nurses during infant illness.

Plans to give access to the full protocol, participant level-data and statistical code {31c}

The full protocol is provided as a supplement. Participant-level data on primary outcomes and statistical code will be made available after publication of trial findings, upon request from the authors.

Oversight and monitoring

Composition of the coordinating center and trial steering committee {5d}

The trial study team, consisting of the PI, site-PI, research coordinators, data manager, pediatrician, neonatologist, epidemiologist, psychologist, Kenyan MOH consultant and research assistant, meet on a weekly basis to provide oversight of the study. The University of Washington serves as the trial coordinating center, providing overall study leadership, data management, ethical compliance, budget management and oversight of study operations. The data management team consists of the data manager, epidemiologist, research coordinator, study coordinator and research assistant who oversee data quality and meet on a weekly basis.

Composition of the data monitoring committee, its role and reporting structure {21a}

The study Data Safety Monitoring Board (DSMB) is composed of 5 researchers in the fields of biostatistics, maternal-child health, pediatrics and mobile health. The DSMB is independent from the sponsor and has no competing interests. No members of the DSMB have ongoing collaborations with the study PI or site PI. The DSMB charter can be found as supplementary data. The study statistician, assisted by study analysts, prepares a closed report comparing outcomes between study arms for review by the DSMB. The DSMB meets twice yearly and submits reports on the open session to the study team and on the open and closed sessions to the funder and study statistician.

Adverse event reporting and harms {22}

An adverse events (AE) in this trial is defined as any untoward occurrence (physical, psychological, social, or economic) in a human subject participating in research, and serious adverse event (SAE) is defined as a pregnancy loss, maternal or infant hospitalization or death. At each study visit, participants are asked if an AE or SAE occurred since the last visit. All participants are also counselled to contact study staff in the event of an AE or SAE. If an SAE is reported by a participant via SMS, self-report, or through a healthcare facility or provider, details surrounding the event are collected by contacting the participant by phone. If an SAE is reported, study staff notify the Kenyatta National Hospital/University of Nairobi ethics review board and PI of the event within 72 hours. Any breaches of privacy or risk of breach of privacy are reported to the University of Washington IRB and Kenyatta National Hospital/University of Nairobi ethics review board within 24 hours. All AE/SAE are reported in regular progress reports to the ethics review board.

Frequency and plans for auditing trial conduct {23}

Trial conduct is monitored by a DSMB which meet every 6 months throughout the study. No other external trial monitoring is planned.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

All changes to the study protocol are submitted for review by the ethics review committees at the University of Washington and Kenyatta National Hospital/University of Nairobi. The DSMB and clinicaltrials.gov record is updated with any updates to data collection or analysis.

Dissemination plans {31a}

Dissemination of study results to health researchers, policymakers, and clinicians has potential to improve prevention strategies for neonatal mortality in Kenya and in other countries. All data collected in this study will be publicly disseminated to key policymakers at county and national level in Kenya, the public health research community in Kenya and through peer reviewed international journals and conferences. Results from the study will be reported no later than one year after the completion date. The study has been registered in ClinicalTrials.gov.

Discussion

The Mobile WACH NEO trial will evaluate the impact of a peripartum two-way SMS intervention on neonatal mortality. The intervention is designed to impact neonatal survival through improved ENC practices, neonatal care-seeking behaviors, and maternal mental health, which will also be measured as secondary outcomes.

SMS has the potential to reach marginalized populations at scale given the expansion of mobile service coverage and widespread access to personal cellular phones. A growing number of programs leverage mobile infrastructure to deliver health information and support in the peripartum period, including several that have been nationally scaled, illustrating their potential public health impact.^{59,60} However, evidence is limited regarding the clinical impact of peripartum SMS interventions, especially on neonatal outcomes.^{61,62} Studies of Mobile WACH and other one- and two-way SMS interventions in the peripartum period have been shown to improve timely initiation of breastfeeding and duration and practice of exclusive breastfeeding.^{51,63,64} Two-way SMS has also been found to be associated with higher ANC attendance and facility delivery, as well as higher post-partum knowledge and care-seeking behavior for treatment of maternal danger signs.^{65–67} Studies measuring the impact of SMS interventions directly on perinatal mortality are limited. Fedha et al. evaluated antenatal SMS visit reminders and pregnancy health information every two weeks and found no effect on neonatal or intrauterine mortality in Kenya, though the study lacked statistical power and the intervention did not extend into the postpartum period.⁶⁸ Lund et al. showed a reduction in perinatal death in Tanzania in participants receiving one-way SMS and phone call vouchers but were not able to isolate the effect of the SMS intervention.⁶⁹

To our knowledge, Mobile WACH NEO is the first study to rigorously evaluate the impact of two-way SMS on neonatal mortality. Moreover, our intervention is unique in its targeting and evaluation of intermediate factors on the causal pathway to neonatal mortality, including maternal knowledge, preventative behavior, care-seeking, and psychosocial health. Use of the IMB conceptual framework to design the intervention and evaluate factors along the causal pathway will allow empirical understanding of factors that determine neonatal outcomes and the mechanisms by which SMS communication may affect them. This addresses critiques that mobile health studies lack emphasis on identifying modifiable components in the pathway that impacts neonatal outcomes.⁶⁹ Inclusion of self-efficacy, social support, and depression as intermediate outcomes undergirds the importance of approaching neonatal interventions in a more holistic approach to determine the impact of maternal psychosocial health on neonatal outcomes.

The Mobile WACH NEO intervention is also designed to be practical in resource-limited settings. The platform facilitates both sending of automated messages to participants and interactive messaging with a nurse. Scheduled messages are sent to participants in bulk, while replies and individually initiated messages are read and responded to by a nurse, creating an efficient system to maximize healthcare worker time in triaging messages. In addition, automated messages are tailored to women's risk factors and current stage of pregnancy with more frequent messaging at times when risk of adverse neonatal outcomes is highest. Finally, this study is conducted in a mix of rural and urban clinics in Kenya to increase generalizability across geographical contexts.

This study has some limitations. While the criteria used to enroll participants into the high-risk tracks are targeted, messages may not always be fully applicable to all participants in every circumstance. Due to feasibility considerations in implementing the intervention, participants are ineligible if they lack daily

access to a Safaricom phone. Phone access in Kenya is now 89%, and Safaricom is the most widely used mobile phone provider in Kenya, but excluding women who lack access to a Safaricom phone may introduce bias.^{35,36} Also, if a participant is unable to read and write SMS messages, their participation in two-way SMS is reliant on an individual who can read the SMS messages to them, so engagement by low-literacy individuals may be more limited. This may reduce generalizability to low-literacy women or those who do not have an individual who can assist them, who may be the women most in need of such an intervention.

Mobile WACH NEO is unique in its approach to evaluate the effect of a semi-automated two-way SMS system on neonatal outcomes, integrate maternal behavioral health with neonatal health, and understand the underlying mechanisms. Rigorously evaluated interventions will provide a stronger evidence base for decisions about scaling mobile health technologies and maximize their impact.

Trial status

Protocol version number and date: Version: 2.2, October 5, 2020

Recruitment and enrollment for the RCT began September 7, 2020. We anticipate completing enrollment by September 2022 and follow up activities by May 2023.

Abbreviations

AE - Adverse Event

DSMB - Data Safety Monitoring Board

EDD - Estimated Delivery Date

ENC – Essential Newborn Care

ID – Identification number

IMB - Information Motivation Behavior

LMP - Last Menstrual Period

MCH - Maternal and Child Health

MOS - Medical Outcomes Survey

MWN - Mobile WACH NEO

PHMRC - Population Health Metrics Research Consortium

RCT – Randomized Controlled Trial

SAE - Serious Adverse Event

SIM - Subscriber Identity Module

SMS – Short Messaging Service

Declarations

Acknowledgements

We acknowledge support from University of Washington's Global Center for Integrated Health of Women, Adolescents, and Children (Global WACH).

Authors' contributions {31b}

KR, JAU, JK, and BW were involved in conception and trial design. EMC was involved in drafting of the article. KR, JAU, and JU were involved in critical revision of the article for important intellectual content. BAR provided statistical expertise. All the authors were involved in final approval of the article.

Funding {4}

The study is funded by the National Institutes of Health, Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) through grant R01HD098105, as well as the National Institute of Mental Health and the Office of the Director through grant K18MH122978 (to KR).

Availability of data and materials {29}

The datasets used and/or analyzed during the current study will be available from the authors on reasonable request by emailing neor01@uw.edu or the corresponding author after initial results have been published.

Ethics approval and consent to participate {24}

Ethics approval was received from the Kenyatta National Hospital/University of Nairobi and the University of Washington ethical review boards.

Consent for publication {32}

Not applicable.

Competing interests {28}

The authors declare that they have no competing interests.

Author details

Keshet Ronen, Department of Global Health, University of Washington

Esther M. Choo, Department of Global Health, University of Washington

Brenda Wandika, Department of Research & Programs, Kenyatta National Hospital

Jenna Udren, Department of Global Health, University of Washington

Lusi Osborn, Department of Research & Programs, Kenyatta National Hospital

Peninah Kithao, Department of Research & Programs, Kenyatta National Hospital

Anna Hedstrom, Departments of Pediatrics and Global Health, University of Washington

Millicent Masinde, Department of Obstetrics and Gynecology, Kenyatta National Hospital

Manasi Kumar, Department of Psychiatry, University of Nairobi

Dalton Wamalwa, Department of Paediatrics & Child Health, University of Nairobi

Barbra A. Richardson, Departments of Biostatistics, Global Health, University of Washington

John Kinuthia, Department of Research & Programs, Kenyatta National Hospital

Jennifer A. Unger, Departments of Obstetrics and Gynecology and Global Health, University of Washington

References

1. WHO. Newborns: reducing mortality. <https://www.who.int/news-room/fact-sheets/detail/newborns-reducing-mortality>. Accessed August 17, 2020.
2. UN Inter-agency Group for Child Mortality Estimation. *Levels & Trends in Child Mortality*; 2019. <https://childmortality.org/wp-content/uploads/2019/10/UN-IGME-Child-Mortality-Report-2019.pdf>.
3. National Bureau of Statistics, Ministry of Health/Kenya, National AIDS Control Council/Kenya, Kenya Medical Research Institute, National Council for Population and Development/Kenya, ICF International. *Kenya Demographic and Health Survey 2014*. Rockville, MD; 2015. www.DHSprogram.com. Accessed October 14, 2020.
4. United Nations. *Global Indicator Framework for the Sustainable Development Goals and Targets*.
5. World Health Organization, UNICEF. *EVERY NEWBORN An Action Plan To End Preventable Deaths*; 2014. www.who.int. Accessed October 14, 2020.
6. WHO. *WHO Recommendations on Newborn Health Guidelines*; 2017.
7. Bhutta ZA, Darmstadt GL, Hasan BS, Haws RA. Community-based interventions for improving perinatal and neonatal health outcomes in developing countries: A review of the evidence. *Pediatrics*.

- 2005;115(2):519-617. doi:10.1542/peds.2004-1441
8. Edmond K, Newton S, Hurt L, et al. Timing of initiation, patterns of breastfeeding, and infant survival: Prospective analysis of pooled data from three randomised trials. *Lancet Glob Heal*. 2016;4(4):e266-e275. doi:10.1016/S2214-109X(16)00040-1
 9. Agrawal PK, Agrawa S, Mullany LC, et al. Clean cord care practices and neonatal mortality: Evidence from rural Uttar Pradesh, India. *J Epidemiol Community Health*. 2012;66(8):755-758. doi:10.1136/jech-2011-200362
 10. Lunze K, Hamer DH. Thermal protection of the newborn in resource-limited environments. *J Perinatol*. 2012;32(5):317-324. doi:10.1038/jp.2012.11
 11. Bee M, Shiroor A, Hill Z. Neonatal care practices in sub-Saharan Africa: A systematic review of quantitative and qualitative data. *J Heal Popul Nutr*. 2018;37(1). doi:10.1186/s41043-018-0141-5
 12. Bogale TN, Worku AG, Bikis GA, Kebede ZT. Why gone too soon? Examining social determinants of neonatal deaths in northwest Ethiopia using the three delay model approach. *BMC Pediatr*. 2017;17(1):216. doi:10.1186/s12887-017-0967-9
 13. Källander K, Hildenwall H, Waiswa P, Galiwango E, Peterson S, Pariyob G. Delayed care seeking for fatal pneumonia in children aged under five years in Uganda: A case-series study. *Bull World Health Organ*. 2008;86(5):332-338. doi:10.2471/BLT.07.049353
 14. Waiswa P, Kallander K, Peterson S, Tomson G, Pariyo GW. Using the three delays model to understand why newborn babies die in eastern Uganda. *Trop Med Int Heal*. 2010;15(8):964-972. doi:10.1111/j.1365-3156.2010.02557.x
 15. Wilmot E, Yotebieng M, Norris A, Ngabo F. Missed Opportunities in Neonatal Deaths in Rwanda: Applying the Three Delays Model in a Cross-Sectional Analysis of Neonatal Death. *Matern Child Health J*. 2017;21(5):1121-1129. doi:10.1007/s10995-016-2210-y
 16. Thaddeus S, Maine D. Too far to walk: Maternal mortality in context. *Soc Sci Med*. 1994;38(8):1091-1110. doi:10.1016/0277-9536(94)90226-7
 17. Alhusen JL, Ayres L, Depriest K. Effects of Maternal Mental Health on Engagement in Favorable Health Practices During Pregnancy. *J Midwifery Women's Heal*. 2016;61(2):210-216. doi:10.1111/jmwh.12407
 18. Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The impact of maternal depression during pregnancy on perinatal outcomes: A systematic review and meta-analysis. *J Clin Psychiatry*. 2013;74(4). doi:10.4088/JCP.12r07968
 19. Jarde A, Morais M, Kingston D, et al. Neonatal outcomes in women with untreated antenatal depression compared with women without depression: A systematic review and meta-analysis. *JAMA Psychiatry*. 2016;73(8):826-837. doi:10.1001/jamapsychiatry.2016.0934
 20. Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Arch Gen Psychiatry*. 2010;67(10):1012-1024. doi:10.1001/archgenpsychiatry.2010.111

21. Gausia K, Moran AC, Ali M, Ryder D, Fisher C, Koblinsky M. Psychological and social consequences among mothers suffering from perinatal loss: Perspective from a low income country. *BMC Public Health*. 2011;11(1):451. doi:10.1186/1471-2458-11-451
22. Murray L, Cooper PJ, Stein A. Postnatal depression and infant development. *Br Med J*. 1991;302(6783):978-979. doi:10.1136/bmj.302.6783.978
23. Deave T, Heron J, Evans J, Emond A. The impact of maternal depression in pregnancy on early child development. *BJOG An Int J Obstet Gynaecol*. 2008;115(8):1043-1051. doi:10.1111/j.1471-0528.2008.01752.x
24. Huizink AC, Robles De Medina PG, Mulder EJH, Visser GHA, Buitelaar JK. Stress during pregnancy is associated with developmental outcome in infancy. *J Child Psychol Psychiatry Allied Discip*. 2003;44(6):810-818. doi:10.1111/1469-7610.00166
25. Beijers R, Jansen J, Riksen-Walraven M, De Weerth C. Maternal prenatal anxiety and stress predict infant illnesses and health complaints. *Pediatrics*. 2010;126(2). doi:10.1542/peds.2009-3226
26. Feldman R, Granat A, Pariente C, Kanety H, Kuint J, Gilboa-Schechtman E. Maternal Depression and Anxiety Across the Postpartum Year and Infant Social Engagement, Fear Regulation, and Stress Reactivity. *J Am Acad Child Adolesc Psychiatry*. 2009;48(9):919-927. doi:10.1097/CHI.0b013e3181b21651
27. McLearn KT, Minkovitz CS, Strobino DM, Marks E, Hou W. The timing of maternal depressive symptoms and mothers' parenting practices with young children: Implications for pediatric practice. *Pediatrics*. 2006;118(1). doi:10.1542/peds.2005-1551
28. Wado YD, Afework MF, Hindin MJ. Effects of Maternal Pregnancy Intention, Depressive Symptoms and Social Support on Risk of Low Birth Weight: A Prospective Study from Southwestern Ethiopia. Bhutta ZA, ed. *PLoS One*. 2014;9(5):e96304. doi:10.1371/journal.pone.0096304
29. Kawachi I, Kennedy BP, Lochner K, Prothrow-Stith D. Social capital, income inequality, and mortality. *Am J Public Health*. 1997;87(9):1491-1498. doi:10.2105/AJPH.87.9.1491
30. Albanese AM, Russo GR, Geller PA. The role of parental self-efficacy in parent and child well-being: A systematic review of associated outcomes. *Child Care Health Dev*. 2019;45(3):333-363. doi:10.1111/cch.12661
31. Bahorski JS, Childs GD, Loan LA, et al. Self-efficacy, infant feeding practices, and infant weight gain: An integrative review. *J Child Heal Care*. 2019;23(2):286-310. doi:10.1177/1367493518788466
32. Leahy-Warren P, McCarthy G. Maternal parental self-efficacy in the postpartum period. *Midwifery*. 2011;27(6):802-810. doi:10.1016/j.midw.2010.07.008
33. Gao LL, Chan SWC, Mao Q. Depression, perceived stress, and social support among first-time Chinese mothers and fathers in the postpartum period. *Res Nurs Heal*. 2009;32(1):50-58. doi:10.1002/nur.20306
34. Warren PL. First-time mothers: Social support and confidence in infant care. *J Adv Nurs*. 2005;50(5):479-488. doi:10.1111/j.1365-2648.2005.03425.x

35. Government of Kenya. *Kenya Integrated Household Budget Survey 2015-2016*; 2018. <http://statistics.knbs.or.ke/nada/index.php/catalog/88>. Accessed August 17, 2020.
36. Communications Authority of Kenya. *ICT Sector Quarterly Statistics Report (January - March 2020)*; 2020. <https://ca.go.ke/wp-content/uploads/2020/07/Sector-Statistics-Report-Q3-2019-2020-.pdf>. Accessed August 17, 2020.
37. Kenya Ministry of Health. *Kenya Standards and Guidelines for MHealth Systems. Report*; 2017. <https://www.health.go.ke/wp-content/uploads/2020/02/Revised-Guidelines-For-Mhealth-Systems-May-Version.pdf>.
38. Kazi AM, Carmichael J-L, Hapanna GW, et al. Assessing Mobile Phone Access and Perceptions for Texting-Based mHealth Interventions Among Expectant Mothers and Child Caregivers in Remote Regions of Northern Kenya: A Survey-Based Descriptive Study. *JMIR Public Heal Surveill*. 2017;3(1):e5. doi:10.2196/publichealth.5386
39. Lee SH, Nurmatov UB, Nwaru BI, Mukherjee M, Grant L, Pagliari C. Effectiveness of mHealth interventions for maternal, newborn and child health in low- and middle-income countries: Systematic review and meta-analysis. *J Glob Health*. 2016;6(1). doi:10.7189/jogh.06.010401
40. Mbuthia F, Reid M, Fichardt A. MHealth communication to strengthen postnatal care in rural areas: A systematic review. *BMC Pregnancy Childbirth*. 2019;19(1). doi:10.1186/s12884-019-2531-0
41. Hussain-Shamsy N, Shah A, Vigod SN, Zaheer J, Seto E. Mobile health for perinatal depression and anxiety: Scoping review. *J Med Internet Res*. 2020;22(4):e17011. doi:10.2196/17011
42. Adanikin AI, Awoleke JO, Adeyiolu A. Role of reminder by text message in enhancing postnatal clinic attendance. *Int J Gynecol Obstet*. 2014;126(2):179-180. doi:10.1016/j.ijgo.2014.02.009
43. Watterson JL, Walsh J, Madeka I. Using mHealth to Improve Usage of Antenatal Care, Postnatal Care, and Immunization: A Systematic Review of the Literature. *Biomed Res Int*. 2015;2015. doi:10.1155/2015/153402
44. Feroz A, Perveen S, Aftab W. Role of mHealth applications for improving antenatal and postnatal care in low and middle income countries: a systematic review. *BMC Health Serv Res*. 2017;17(1):704. doi:10.1186/s12913-017-2664-7
45. Lund S, Hemed M, Nielsen BB, et al. Mobile phones as a health communication tool to improve skilled attendance at delivery in Zanzibar: A cluster-randomised controlled trial. *BJOG An Int J Obstet Gynaecol*. 2012;119(10):1256-1264. doi:10.1111/j.1471-0528.2012.03413.x
46. Unger JA, Wandika B, Ronen K, et al. Mobile WACH NEO: Engagement of pregnant and postpartum women with a two-way SMS service to improve neonatal outcomes. In: *Pediatric Academic Society*. Baltimore, MD; 2019.
47. Sondaal SFV, Browne JL, Amoakoh-Coleman M, et al. Assessing the effect of mHealth interventions in improving maternal and neonatal care in low- And middle-income countries: A systematic review. *PLoS One*. 2016;11(5). doi:10.1371/journal.pone.0154664
48. WHO. *WHO Guideline: Recommendations on Digital Interventions for Health System Strengthening*. World Health Organization; 2019. <http://www.who.int/reproductivehealth/publications/digital->

- interventions-health-system-strengthening/en/. Accessed August 17, 2020.
49. Zhou C, Hu H, Wang C, et al. The effectiveness of mHealth interventions on postpartum depression: A systematic review and meta-analysis. *J Telemed Telecare*. April 2020:1357633X2091781. doi:10.1177/1357633X20917816
 50. Fisher WA, Fisher JD, Harman J. The information-motivation-behavioral skills model: A general social psychological approach to understanding and promoting health behavior. In: Suls J, Wallston KA, eds. *Social Psychological Foundations of Health and Illness*. John Wiley & Sons; 2003:82-106. doi:10.1002/9780470753552.ch4
 51. Unger JA, Ronen K, Perrier T, et al. Short message service communication improves exclusive breastfeeding and early postpartum contraception in a low- to middle-income country setting: a randomised trial. *BJOG An Int J Obstet Gynaecol*. 2018;125(12):1620-1629. doi:10.1111/1471-0528.15337
 52. Drake AL, Unger JA, Ronen K, et al. Evaluation of mHealth strategies to optimize adherence and efficacy of Option B+ prevention of mother-to-child HIV transmission: Rationale, design and methods of a 3-armed randomized controlled trial. *Contemp Clin Trials*. 2017;57:44-50. doi:10.1016/j.cct.2017.03.007
 53. Harrington EK, Drake AL, Matemo D, et al. An mHealth SMS intervention on Postpartum Contraceptive Use among Women and Couples in Kenya: A randomized controlled trial. *Am J Public Health*. 2019;109(6):934-941. doi:10.2105/AJPH.2019.305051
 54. Kenya Ministry of Public Health and Sanitation. *National Guidelines on Essential Newborn Care*. Nairobi, Kenya; 2015.
 55. Unger JA, Kinuthia J, John-Stewart G. Texting Condolences: Adapting mHealth Programs After Unexpected Pregnancy and Infant Outcomes. *JMIR mHealth uHealth*. 2017;5(12):e176. doi:10.2196/mhealth.8303
 56. Perrier T, Dell N, DeRenzi B, et al. Engaging pregnant women in Kenya with a hybrid computer-human SMS communication system. In: *33rd Annual ACM Conference*. New York, New York, USA: ACM Press; 2015:1429-1438.
 57. Murray CJL, Lopez AD, Black R, et al. Population Health Metrics Research Consortium gold standard verbal autopsy validation study: Design, implementation, and development of analysis datasets. *Popul Health Metr*. 2011;9(1):27. doi:10.1186/1478-7954-9-27
 58. Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *J R Stat Soc Ser B*. 1995;57(1):289-300. doi:10.1111/j.2517-6161.1995.tb02031
 59. LeFevre AE, Dane P, Copley CJ, et al. Unpacking the performance of a mobile health information messaging program for mothers (MomConnect) in South Africa: Evidence on program reach and messaging exposure. *BMJ Glob Heal*. 2018;3(Suppl 2):583. doi:10.1136/bmjgh-2017-000583
 60. Evans WD, Wallace JL, Snider J. Pilot evaluation of the text4baby mobile health program. *BMC Public Health*. 2012;12(1). doi:10.1186/1471-2458-12-1031

61. Mehl GL, Tamrat T, Bhardwaj S, Blaschke S, Labrique A. Digital health vision: Could MomConnect provide a pragmatic starting point for achieving universal health coverage in South Africa and elsewhere? *BMJ Glob Heal*. 2018;3(Suppl 2):626. doi:10.1136/bmjgh-2017-000626
62. Whittaker R, Matoff-Stepp S, Meehan J, et al. Text4baby: Development and implementation of a national text messaging health information service. *Am J Public Health*. 2012;102(12):2207-2213. doi:10.2105/AJPH.2012.300736
63. Jiang H, Li M, Wen LM, et al. Effect of short message service on infant feeding practice findings from a community-based study in shanghai, china. *JAMA Pediatr*. 2014;168(5):471-478. doi:10.1001/jamapediatrics.2014.58
64. Flax VL, Negerie M, Ibrahim AU, Leatherman S, Daza EJ, Bentley ME. Integrating group counseling, cell phone messaging, and participant-generated songs and dramas into a microcredit program increases Nigerian women's adherence to international breastfeeding recommendations. *J Nutr*. 2014;144(7):1120-1124. doi:10.3945/jn.113.190124
65. Omole O, Ijadunola MY, Olotu E, et al. The effect of mobile phone short message service on maternal health in south-west Nigeria. *Int J Health Plann Manage*. 2018;33(1):155-170. doi:10.1002/hpm.2404
66. Bangal VB, Borawake SK, Gavhane SP, Aher KH. Use of mobile phone for improvement in maternal health: a randomized control trial. *Int J Reprod Contracept Obs Gynecol*. 2017;6(12):5458-5463. doi:10.18203/2320-1770.ijrcog20175260
67. Jones RM, Kimenju G, Subbiah S, Styles A, Pearson N, Rajasekharan S. A Short Message Service (SMS) increases postpartum care-seeking behavior and uptake of family planning of mothers in peri-urban public facilities in Kenya. *PLoS One*. 2020;15(9 September). doi:10.1371/journal.pone.0239213
68. Fedha T. Impact of Mobile Telephone on Maternal Health Service Care: A Case of Njoro Division. *Open J Prev Med*. 2014;04(05):365-376. doi:10.4236/ojpm.2014.45044
69. Lund S, Rasch V, Hemed M, et al. Mobile phone intervention reduces perinatal mortality in zanzibar: Secondary outcomes of a cluster randomized controlled trial. *J Med Internet Res*. 2014;16(3). doi:10.2196/mhealth.2941

Figures

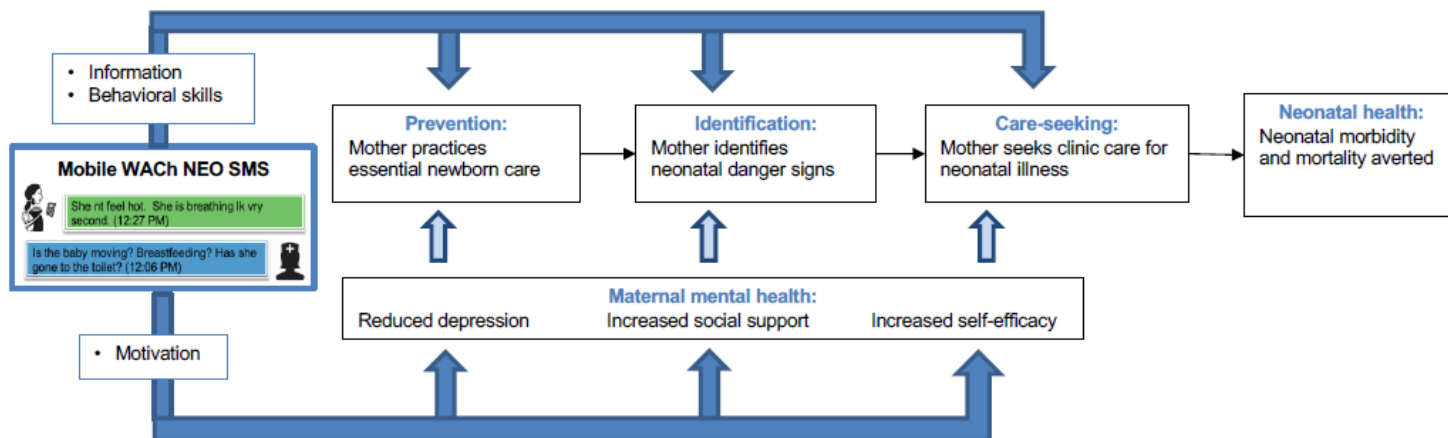


Figure 1

Conceptual framework for Mobile WACH NEO

Timing	28-36 weeks pregnant	38 weeks pregnant	Delivery	2 weeks postpartum	6 weeks postpartum
Messaging frequency	1/week	1/day	2/day*	1 every other day	
Messaging topics	Facility based delivery Birth planning				
	Essential newborn care				
				Family planning	
	Anticipatory guidance of neonatal and maternal danger signs		Identification of neonatal and maternal danger signs		
	Social and emotional support				
Tracks ⁴	Pregnancy loss ⁵		Infant death ⁵		
			Preterm birth (<37 weeks gestation) or Low birthweight (<2500g) ¹		
	Depressive symptoms (EDPS score ≥ 13) ²				
	Adolescent (≤19 years old) or first-time pregnancy ³				
	General				

* One message on a topic, the second message on screening for a danger sign

¹ Track placement triggered at delivery and 2-week study visit

² Track placement triggered at enrollment and 2-week study visit

³ Track placement triggered at enrollment

⁴ Additional messages sent to participants placed in tracks

⁵ Track placement triggered immediately when study learns of pregnancy loss or infant death

Figure 2

Messaging timing, content and tracks for Mobile WACH NEO

Send Msg

Call Log 0

✓ Nurse

Displaying Translated

6 Mar 18 13:22

Sorry Mariane, It might be the baby is sick please seek medical attention as soon as possible.

Mariane

Displaying Translated

infant-health

6 Mar 18 13:08

Am Mariane baby is crying and has fever what can be the cause?

Reply

✓ System

Displaying Original

ddd.two-way.normal.61

5 Mar 18 13:05

Mariane , mae en Mercy mawuok Rachuonyo.(name), mae en (nurse) Yuak mar nyathi nyalo kelo paro ne jonyuol. Ka nyathini yuak ahinya molooyo saboro kata godhiambo nyalo bedo ni iye rame. Tem ikete konindo auma e bamni ti rudhone ne toke kata inyalo kete badi kawie ong'lo piny ti swuoye. Nyiswa kineno magi kendo kidwaro puonj moko.

✓ Nurse

Displaying Translated

5 Mar 18 9:37

congradulations'

Mariane

Displaying Translated

delivery-concerns

4 Mar 18 11:41

iam Mariane i delivered well rachuonyo

Reply

Mariane

Displaying Original

other

4 Mar 18 11:15

An Mariane ne

Reply

Participant Details: Getrude

Edit

Phone number

Estimated Delivery Date

Delivery Date

Age 28

Send Time Afternoon (1 PM)

Previous pregnancies 3

Confirmation Code 11521

Clinic Visits and History

Visit History

Date	Type	When	
2018-04-11	Study Visit	2w	<div>Attended</div> <div>Del</div> <div>Edit</div>

Other Actions

Notes 1

Stop

Figure 3

Screenshot of Mobile WACH system study nurse interface

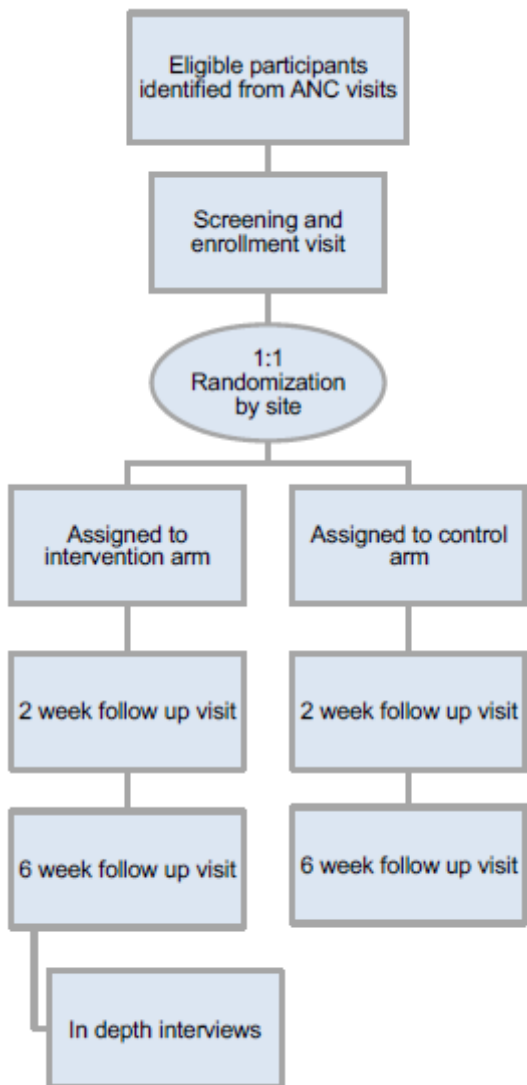


Figure 4

CONSORT diagram of Mobile WACH NEO Trial. ANC indicates antenatal care.