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Title: Wireless Physiologic Monitoring in Postpartum Women

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Background and Significance
Between 1990 and 2015, global maternal mortality dropped by 45%, from 532,000 deaths per year to an estimated 303,000.[1,2] While encouraging, too many women continue to die in childbirth. At current projections, an estimated 3.8 million maternal deaths will occur between now and 2030, with the majority (66%) in sub-Saharan Africa.[1,2] Maternal mortality rates in Uganda mirror global patterns. Currently the life time risk of maternal death in Uganda is still as high as 1 in 47 compared to rates of 1 in 6,000 in resource rich countries.[1]

Most maternal deaths occur immediately around childbirth [3] and approximately 45% in the first 24 hours.[4] As such, the promotion of facility-based childbirth has been a corner stone of strategies to reduce maternal and neonatal deaths in low and middle-income countries.[5,6] However, despite increases in the proportion of women delivering at facilities, reductions in mortality and morbidity have not been as rapid as expected.[5] Evidence points to delays at the facility in the recognition of complications and timely intervention as once cause of morbidity and mortality.[7-12] Recognizing the critical timeframe in the immediate postpartum period, current guidelines from WHO call for close monitoring during this time.[13] Similarly, nursing standards in resource-rich settings recommend physiologic monitoring every 15 minutes for the first 2 hours postpartum, then every fours for the first 24 hours.[14 15] Sustaining such high frequency monitoring remains a challenge even in resource-rich settings.[16 17] In RLS contexts such as Mbarara, Uganda, where staff-to-patient ratios may be as high as 1:50,[18] such normative standards around monitoring are unattainable with current systems of physiologic monitoring.

Abnormalities in physiologic signs have been shown to predict subsequent in-hospital mortality and morbidity amongst emergency department and medical ward patients.[19-23] In response to these findings, health care systems in resource-rich settings have introduced “Track and Trigger” protocols and “Early Warning Scores” to identify abnormalities in physiologic signs and activate appropriate responses.[24] In the case of heart disease, combining early warning of potential illness with

appropriate medical response has reduced rates of cardiac arrest, readmissions to critical care, and mortality.[25-27] Similar strategies have been recommended in an obstetric setting, where the most common causes of mortality are hemorrhage, hypertensive disease, and sepsis, accounting for 27.1%, 14.0% and 10.7% of maternal deaths worldwide.[28] These conditions are commonly associated with abnormal physiologic signs– hemorrhage causing tachycardia and hypotension; pre-eclampsia/eclampsia causing hypertension and hypoxia; and sepsis causing fever, tachycardia, hypotension, and hypoxia.[29,30]

We have previously studied the feasibility and preliminarily tested the acceptability of using a wireless biosensor (BioPatch™) to capture physiologic signs over 30 minutes in 50 healthy non-laboring pregnant women, and transmit this data to a central monitor (ZephyrLIFE™) at the Mbarara Regional Referral Hospital (MRRH).[18] The biosensor is compact and round, with a diameter of 4cm, attached to the chest with standard adhesive electrodes (Figure 1). The sensor captures HR based on the R-R interval of a single lead electrocardiogram, RR (via impedance), and estimates core temperature based on HR variability. Data from the sensor is transmitted to a central monitor over a wireless network. Software at the central monitor enables reception of data, and customizable on-screen and audible alarts . The sensor is approved by the US Food and Drug Administration for general adult use. Our studies of feasibility demonstrated functionality of the biosensor, with >80% of physiologic sign capture in the MRRH setting.[18,31] We also found that with minimal training, clinicians in at MRRH were able to correctly apply the biosensor, input participant information into the central monitor and track output of data. Additionally, women wearing the device found it comfortable and useful. We will be building on this preliminary work and experience to test the impact of wireless monitoring on clinical outcomes.

Specific Aims

1. To estimate the clinical effectiveness of wireless physiologic monitoring of women in the first 24 hours after emergency cesarean delivery at Mbarara Regional Referral Hospital (MRRH)
2. To evaluate the clinical adoption of wireless physiologic monitoring at MRRH using an implementation science approach.
3. To use qualitative methods to explore clinical adoption and acceptability of wireless physiologic monitoring among postpartum women at MRRH and understand facilitators and barriers to uptake of wireless physiologic monitoring.
4. To estimate the cost of providing wireless physiologic monitoring of women in the first 24 hours after emergency cesarean delivery at MRRH
5. To estimate the incremental cost-effectiveness, measured as cost per severe maternal outcome adverted using wireless physiologic monitoring compared to current standard of care monitoring.
6. To explore the ethical considerations of obtaining intrapartum consent among women enrolling in this study
7. To evaluate if motion in the early post-operative period is related to functionality, mobility and wellness during recovery from cesarean delivery and how recovery relates to financial risks after cesarean delivery.

Methodology

Setting: The research will be carried out in the Department of OB/GYN MRRH in Mbarara, Uganda. This facility is the primary referral hospital in southwest Uganda. It performs ~ 10,000 deliveries per year (~ 30/day), has a maternal mortality ratio of 460 per 100,000 live births (~50-60 deaths per year)

and a cesarean delivery rate of 40%. All women delivered by cesarean are followed and monitored by postgraduate doctors with assistance from midwives. In this facility, postgraduate doctors complete medical training including a two-year internship and practice independently for several years prior to postgraduate training in OB/GYN. Consultant/Specialist OB/GYN supervisors oversee clinical care from home or in-hospital depending on clinical acuity There are currently 13 consultants/specialists, 39 postgraduate doctors in the institution, and 40 midwives with clinical privileges in the department. The physician to patient ratio ranges from 1:8 during the day to 1:25 during the night and weekends.

Study Population:
The following types of participants will be recruited for study purposes:
1) Clinicians: Consultants/Specialists and nurse/midwives with clinical duty on the maternity ward at MRRH during the study period.
2) Peripartum women delivered by emergency cesarean during the study period.

Study Intervention:
The intervention in this study is the use of a wireless monitor to perform physiologic monitoring of women undergoing emergency cesarean delivery for the first 24 hours after completion of the cesarean.
The wireless monitor to be used is a wearable wireless vital sign monitor called Current ™. The device provides continuous real-time transmission of oxygen saturation, respiration rate, pulse rate, temperature, motion and activity, and posture captured every 2 seconds. It is integrated with the Omron Evolv blood™ pressure cuff to allow automated capture of blood pressure. Physiologic data from the sensor is transmitted via WiFi to a secure cloud storage (hosted by Amazon Web Services). Current™ is fully HIPAA [1]compliant and HITrust[2] certified and has received US FDA approval. Physiologic data can then be accessed via a secure password protected mobile phone app or displayed on a monitor for real-time viewing. Pre-defined criteria can be used to program alerts or notifications should vital signs fall outside of the range. These notifications can be received via SMS or a mobile app notification. Notifications can be sent to multiple providers at a time. Providers can also log on or off from the device corresponding to their duty shifts.

To complete Aim 1, we will enroll all willing attending doctors and staff midwives with clinical duties covering the maternity ward, emergency cesarean delivery and postoperative care during the study period to use the wireless physiologic system and receive message alerts. Due to staffing the numbers of clinicians may fluctuate during the enrollment period We will also enroll 1235 women undergoing emergency cesarean delivery during the study period during intervention blocks to wear a wireless physiologic monitor for 24 hours after birth. An additional 1235 women, also undergoing emergency cesarean during the study period during non-intervention blocks, will form a control group and have medical record review only. *We request to waive consent for this record review only.* Clinicians and peripartum women participating in wireless physiologic monitoring will form the same participants for Aim 2, which will involve participant observation, record review, and retrieval of data from the wireless monitoring system and clinician responder phones. To complete Aim 3, We will perform semi-structured interviews on 30 clinicians and 30 postpartum women drawn from

[1] HIPAA: Health Insurance Portability and Accountability Act of 1996) is United States legislation that provides data privacy and security provisions for safeguarding medical information

[2] **HITRUST**, in collaboration with private sector, government, technology and information privacy and security leaders, has established the **HITRUST** CSF, a certifiable framework that can be used by any organization that creates, accesses, stores or exchanges sensitive information. The framework provides a way to comply with HIPAA standards

those participants enrolled in Aim 1 and 2. To complete Aim 4 and 5 activity-based costing will be used to identify the main activities, resources and specific inputs used to support implementation of the wireless monitoring system and current standard of care. Time-based tracking will be used to perform time and motion studies to determine the time and processes to implement the monitoring system. To complete Aim 6, women will be administered a pain and anxiety assessments, as well as assessment of trust in medical providers, and a questionnaire assessing the quality of the informed consent process. 15-20 women consent and 15 women declining will be invited to participate in a semi-structured interview (drawn from participants in Aim 1, and not including any women participating in Aim 2).

Study Population Overview

Participants	Activities	Consent	Total Number
Midwives and consultant/specialists	Placement of monitors on enrolled women; Hold responder phone for possible text alerts; In-depth interviews (30 clinicians)	Yes	~ 52
Peripartum women	Wear wireless monitor for 24 hours after delivery Record review; Semi-structured interviews (30 women)	Yes	1235
Peripartum women (controls)	Record review only	No	1235
Total Study Population			**2522**

Subject Selection

Clinicians

Inclusion Criteria	Rationale
1. Clinical privileges at MRRH	Given this is a hybrid efficacy-implementation trial, the research aims require integration of the intervention into routine clinical care. As such and for logistical purposes we will recruit those clinicians who will be providing clinical care to participants.
2. Clinical duty during study period	The research intervention will require clinicians to receive alerts of potentially critically ill participants, however we will not provide guidance on management or the appropriate clinical intervention. As such we require that all clinicians enrolled have sufficient experience to provide appropriate clinical care for women should that be required.
3.	
Exclusion criteria	**Rationale**
1. Inability to speak English or Runyankole	Lack of available interpreters for effective communication in other languages; It is anticipated 100% of clinicians at this facility speaks one of these two languages

Peripartum Women

Inclusion criteria	Rationale
1. Age >18	We will exclude women under the age of 18 because even if they are considered emancipated minors, most are not adults physiologically. Our research questions are designed to study physiologic monitoring in adult women, and may not apply equally to pregnant children under the age of 18. Moreover, this the wireless device currently only has food and drug safety approval for adult use.
2. Undergoing emergency cesarean delivery at MRRH	Women undergoing emergency cesarean are chosen due to increased risk of morbidity and mortality in this population. Additionally, the study proposes to test monitoring in the first 24 hours after birth, therefore women delivered outside of MRRH and arriving in the postpartum period will arrive after this period has begun and will miss the critical window to initiate monitoring.

3. Able to provide consent or have a guardian/attendant present who can consent on their behalf.	The latter is included as monitoring critically ill women who may be unable to provide their own consent is paramount to ultimately affecting clinical outcomes
4. Willing to wear the biosensor for 24 hours	Wearing the monitor is integral to the proposed intervention. Given the technical capabilities of the monitor, current wireless signals will only be available on the postpartum ward, therefore women will need to be present on the ward for the device to transmit signals to the central monitor and alerts to clinicians should abnormalities occur.
5. Willing to remain in the postpartum unit for 24 hours	
Exclusion Criteria	**Rationale**
1. Admitted to ICU directly after delivery	The ICU at MRRH is a closed unit in a separate building from the postpartum ward, as such, monitoring systems in use there are different from on the postpartum ward. The aim of this study is to investigate the use of wireless monitoring for women admitted to the postpartum ward after delivery.
2. Known allergies or hypersensitivity to device materials	For this research we will be limited to using standard electrode adhesives to apply the device. To avoid adverse reactions, any women with allergies or known hypersensitivity to the device will be excluded.
3. Scheduled or Elective Surgery	Excluded due to the decreased morbidity in this population.
4. In ability to speak English or Runyankole	Lack of available interpreters for effective communication in other languages; It is anticipated >95% of the local population at this facility speaks one of these two languages

Subject Enrollment and Consent Procedures

1. **Clinicians:** Prior to the initiation of the study, a group meeting will be held with clinicians (midwives and specialists/consultants) explaining the background of the study, rationale of the study and anticipated study procedures. This meeting will be timed to be held during routine maternity administration time to avoid impacting clinical activities. Clinicians who are interested in the study will then be approached individually and given more details on the study procedures, and the potential risks and benefits. A trained member of the research team will be responsible for conducting this consent. The PI will oversee the consenting process but not participate directly to avoid any potential conflicts and unintended pressure on clinicians to participate. The trained team member will approach participants, introduce the study, and gauge interest. S/he will explain study procedures to the doctor and include potential risks and benefits. Consents will be written to maximize understanding of the study procedures and potential risks and to comply with standards in place by MUST ethical review committee and Partners institutional review board. Clinicians who agree to participate will sign consent in the language of their choice (English or Runyankole). A copy of the consent will be given to the participant. Information on how to contact study staff, report adverse events or concerns associated with study will be provided on the consent forms. Clinicians will have over 24 hours from explanation of the study with risks and benefits to choose to participate or not and sign informed consent.

2. **Peripartum women:** To enable wireless monitoring to begin immediately or as soon as possible after cesarean delivery, the RA will approach *all* women waiting in labor or registering for delivery during the study period. Women cannot be approached prior to presentation for delivery due to logistical constraints with patient scheduling and follow-up in this setting. The RA will screen for eligibility and explain the study to eligible women and obtain assent for potential inclusion. Women will only be enrolled if the decision is made for an emergency cesarean

delivery during their labor or antepartum course. This decision will be made per the standard of care in the clinic and not influenced by research goals or procedures

In a private space, potential participants will have the study and study procedures described verbally in their preferred language (English or Runyankole) and given written information about the study in their preferred language. The RA recruiting and seeking consent will be carefully trained to fully explain the risks and benefits and to ensure women understand that they will still receive current standard of care at the hospital should they decline to participate in. Prior to describing the study and study procedures the RA will conduct a pain assessment using the facies and numerical pain scale and anxiety assessing using the State Trait Anxiety Scale (Appendix 10)

It will be clearly explained to women that actual enrollment will occur if the decision is made for an emergency cesarean delivery and that study explanation is being done ahead of time due to the due to the nature of childbirth with an unpredictable timing for a decision for emergency cesarean delivery, and often need for urgent medical care and the potential for a high level of emotional and physical stress at that time. For all women who provide assent, the RA will obtain written consent to study enrolment immediately after informed consent for the cesarean delivery has been obtained by the overseeing doctor performing the cesarean.

All consents will be translated into Runyankole and back translated to English. Consent forms will be read aloud in their entirety to potential participants. Women will be informed that participation is voluntary, there are no repercussions for not participating, and they can drop out at any point also without repercussion.

Research assistants will be asked to document field notes at the time of consent to capture information on the length of time taken for the consent, if the participant had others present, and observations during the process of the consent (e.g. discussion by the participant with an attendant or family member)

If women are unconscious or in a mental state where they are unable to consent for themselves, an attendant or guardian will be approached for consent. As women in this condition are at high risk for morbidity and/or mortality inclusion in this study is key to achieve the objectives of reducing this risk. Additionally, women in this condition are the most likely to gain direct benefit from vital sign monitoring. As such if an attendant is not available the woman will be enrolled without consent to enable monitoring to begin immediately. Consent will be sought as soon as possible after the woman regains capacity to consent or an attendant becomes available. If the woman and/or her attendant declines to participate at that time all study procedures will be discontinued.

Study Procedures

1. A group meeting detailing the study background, procedures, risks and benefits will be held for all clinical providers in the department prior to study initiation.
2. We will obtain informed consent for clinicians and peripartum women admitted for delivery as described above.
3. A 2-hour training session on the use of the wireless monitoring system, nature of alerts and emergency mobile phone will be held for enrolled clinicians at a time convenient to them.
4. Alternative two-week blocks will be assigned to “intervention” vs “control”. During an “intervention block” all women delivering by emergency cesarean and consenting to participate will be monitored using the wireless device for the first 24 hours after delivery. During a “control

block" standard of care for monitoring will be used and women delivering via emergency cesarean will have record review only.

5. Maternity ward coverage schedules for enrolled specialist and midwives will be obtained. This will be used to determine the clinicians on call during each intervention block.

6. During the intervention block, midwives present in the theatre will be asked to perform the following tasks for any emergency cesarean deliveries s/he is present for:

   a. Placement of the biosensor on any enrolled women s/he delivers by emergency cesarean delivery immediately after completion of the surgery.

   b. Input postpartum women's data (name, age, medical identification number) into the central monitor of the monitoring system. This is anticipated to take 1-2 minutes once enrolled midwives have received training on the system. The central monitor will require password access and only clinicians trained in the use of the system and responsible for the care of participants will be provided with password access.

   c. <u>If a midwife is not available in the theatre, a research assistant will perform the above tasks.</u>

7. <u>At a convenient time after consent that does not interfere with clinical care, height, weight and arm circumference will be measured by an RA.</u>

8. Physiologic sign data from the biosensor worn by enrolled women will be automatically transmitted via cellular networks to the central monitor for display. As above, this information will be password protected. Physiologic data will also be available in a stored format on the device (for up to 6 hours) and in cloud storage. Once physiologic data is no longer needed for the clinical care of postpartum women, all data on the cloud storage will be de-identified – within 24-48 hours after monitoring is complete. Participants will be assigned a code to link physiologic data to clinical data performed through record review. Enrolled postpartum women will be given a participant study identification number. All data downloaded from the central monitor or biosensor will be de-identified and study numbers used to link data to participants. All data will be stored on encrypted password protected storage.

9. Call schedules will also be used to determine specialist and midwives responsible for postpartum care of women during the intervention block. Midwives will be asked to hold an assigned emergency mobile phone to which alerts would be sent if abnormalities occur in the physiologic signs of enrolled women. This mobile phone will require password/pin access which will only be given to the enrolled clinicians. Specialists/consultants will also have the option to install a password protected mobile app to receive notifications and alerts and visualize data on their personal mobile phones as long as their phones meet minimum security and privacy measures (password protected and encrypted phone). Enrolled attending physicians with clinical responsibility during the intervention block will also be given the option to receive alerts to their personal mobile phones should abnormalities occur. Alerts will be sent to the emergency mobile phone and personal phones of enrolled specialists who mark themselves as on duty if any of abnormalities occur in physiologic signs as described in Table 1.

Table 1: Predefined limits for clinician alerts

Physiologic sign	Cut off for alert
Heart rate (beats per minute), noted for >5 minutes	>120
Systolic Blood pressure (mmHg), any	>160 or <70
Diastolic blood pressure (mmHg), any	>110 or <30
Temperature (C) noted for >2 minutes	>40C
Respiratory Rate (breaths per min) noted for >5 minutes	>30

Alert messages will include the following text:

- Medical identification number and name

(to allow the covering doctor to find and review relevant clinical information for the patient and fine the patient if needed.

- Nature of abnormality e.g. Heart Rate = 140bpm, or Blood pressure= 180/110. Any clinical response to the abnormality will be left to the discretion of the covering doctor in accordance to current standard care guidelines at MRRH.

10. For clinical safety of the women participants, midwives receiving any alerts indicating the above vital sign abnormalities will be asked to inform one of the doctors on call. In the event of technical issues with the monitoring system, midwives will be able to access a research assistant who will be on 24 hours a day.
11. Every 24 hours a research assistant will perform medical chart review on enrolled participants to assess for documentation of the occurrence of any severe maternal outcome (Table 2). The research assistant will also review daily 24-hour reports generated by covering clinicians (standard maternity ward practice) to identify potential severe maternal outcomes not documented in the medical record.

Table 2: Severe Maternal Outcomes based on WHO Near Miss Criteria with demonstrated feasibility of collection in a RLS[28,29,71]

Outcome	Definition/Measurement
Death	Mortality occurring at any time point after delivery and prior to discharge
Clinical based near-miss criteria	
Acute cyanosis	Blue or purple coloration of the skin or mucous membranes due to low oxygen saturation
Gasping	Terminal respiratory pattern, the breath is convulsively and audibly caught.
Severe bradypnea or tachypnea	Respiratory rate < 6 or Respiratory rate > 40
Shock	Persistent systolic BP ≤ 80 mmHg or a persistent systolic BP ≤ 90 mmHg with a HR ≥ 120.
Oliguria	Urinary output < 30 ml/hour for 4 hours or < 400 ml/24 hours non-responsive to fluids/diuretics.
Failure to form clots	Bedside clotting test or absence of clotting from the IV site after 7 minutes
Prolonged unconsciousness	Complete or near-complete lack of responsiveness to external stimuli.
Cardiac arrest	Sudden absence of pulse and loss of consciousness.
Stroke	Neurological deficit of cerebrovascular cause persisting ≥ 24 hours.
Uncontrollable fits	Refractory, persistent convulsions or status epilepticus.
Total paralysis	Complete or partial paralysis of both sides of the body.
Jaundice in the presence of pre-eclampsia	BP > 140/90) with proteinuria (> 1 + dipstick in ≥ 2 samples) and jaundice.
Laboratory-based near miss criteria	
Acute severe azotemia	Creatinine > 300 mmol/l or > 3,5 mg/dl
Severe acute hyperbilirubinemia	Bilirubin > 100 µmol/l or > 6.0 mg/dl.
Severe acute thrombocytopenia	<50 000 platelets/ml
Management-based near-miss criteria	
Use of continuous vasoactive drugs	Uninterrupted infusion of dopamine, epinephrine, or norepinephrine.
Hysterectomy	Surgical removal of the uterus following infection or hemorrhage.
Massive transfusion	Transfusion of ≥ 5 units of blood
Intubation and ventilation not related to anesthesia	Placement of an endotracheal tube or ventilation for > 60 minutes purposes other than anesthesia
Dialysis for acute renal failure	
Cardiopulmonary resuscitation	Emergency procedures including chest compressions and lung ventilation.

12. The research assistant will also extract data on (age, district of origin, education level, occupation, referred in from another facility), obstetric history (parity, gestational age at delivery, antenatal complications) and medical comorbidities (HIV, chronic hypertension, cardiac, pulmonary or kidney disease). Information on timing of delivery, indication for cesarean

delivery and decision to incision time for emergency caesarean delivery, documentation of physiologic signs will also be extracted. *See Appendix 1 – Chart Review*

13. At the end of each clinical duty or shift enrolled midwives and specialist doctors will be asked to complete a brief questionnaire which will be administered via electronic survey using redcap survey on the responder phone. This will be to assess if the midwife received any alerts, how they responded and if it influenced clinical management. *See Appendix 2 – Call Duty Follow up Questionnaire. This is estimated to take ~5-10mins to complete*.

14. Up to 30 enrolled clinicians who participated in the monitoring system will also be approached at a convenient time for a in depth interview. We will also approach other key stakeholders including clinicians in leadership positions who may not have participated in the monitoring system. These interviews are intended to gather qualitative data on the facilitators and barriers to use and uptake of the monitoring system. Purposively sampling will be used to approach midwives with high use of the system and low use of the system. *See Appendix 3 – Clinician Interview guide.* Interviews will occur in a private room. Interviews will occur at a time convenient to clinicians (within one week of interaction or observation with the wireless monitoring system) so as not to interrupt clinical care. A digital recorder will be used to record interviews and the trained research assistant will then transcribe and translate interviews administered to clinician and post-partum women participants.
15. During the study period approximately 20 of the enrolled midwives will be observed using the wireless monitoring system to determine time performed to perform the steps for initiating monitoring for a woman. *See Appendix 5 – Time Tracking Form.*
16. At the end of 24 hours of monitoring each enrolled woman who participated in monitoring will have a brief structured questionnaire on the acceptability of the monitoring, which will be administered by the research assistant. See Appendix 4 – Postpartum Woman Acceptability Questionnaire. This is estimated to take ~15 minutes.
17. Up to 30 enrolled women will be asked to participate in an in-depth interview on the experience of wearing the wireless monitor. This is conducted to provide context to the above quantitative measures and to understand acceptability and facilitators and barriers to uptake of wireless physiologic monitoring. Women will be purposively sampled for age (18-34 and >35 years) and level of use of the monitor (~15 women who completed 24 hours of monitoring and ~ 15 women with less than 24 hours of monitoring). Interviews will be conducted until thematic saturation is reached. *See Appendix 6 – Postpartum Woman Interview Guide.* This interview is estimated to take ~45 minutes. Interviews will occur in a private room, and prior to discharge but after wireless monitoring is complete (postpartum day 2 and 3 at a time convenient to women. A digital recorder will be used to record interviews and the trained research assistant will then transcribe and translate administered to clinician and post-partum women participants.
18. After these study procedures are complete women will be approached to complete the medical trust researcher scale (Appendix 11) and the QuiC scale (Appendix 12). Additionally, the pain assessment and state trait scale will be repeated (Appendix 10 and 11).
19. Up to 15 enrolled women (distinct from those participating in step 17 above) will be invited to participate in an in-depth interview (Appendix 13) to explore their experiences of going through the informed consent process. Up to 15 women who declined monitoring will be invited to participate in the in-depth interview only (no monitoring) (Appendix 15). A separate consent form will be used for these women (Appendix 14)
20. After every 24 hours of monitoring, data from biosensors which includes continuous physiologic sign data, start and stop time of monitoring and potential interruptions will be downloaded by the research assistant into a secure database. Data from the emergency cellular phone including number of alerts received, time received and time read will also be downloaded and extracted from the cellular phone.
21. The research assistant will also document any external factors that may affect monitoring every 24 hours e.g. electricity outages or cellular network disruptions, and stock outs

22. After discharge, all patients who completed at least 12 hours of monitoring will receive an invitation to complete a short mobile phone survey to measure functionality, mobility, and wellness at day 1, and at 2,4,6 and 12 weeks post discharge (Appendix 16). At 6 weeks post discharge they will also receive survey assessing for health expenditure, depression and postpartum complications (Appendix 17). The questionnaire will be administered by an automated mobile phone survey system , that allows the participants to receive a prerecorded voice call with the survey and instructs them on answer choices. This will be administered through Engage Spark. EngageSPARK is a social enterprise that offers a browser-based, cloud-hosted platform used to launch interactive Voice IVR and SMS text message campaigns globally. This platform has previously been used in studies of providing airtime incentives to survey participants in Uganda as well as Bangladesh and Colombia. A research assistant will call participants to administer the survey for participants unable to access or complete automated phone surveys. Up to 5 attempts will be made to reach the participant to complete the survey. Participants will receive instruction from a RA on the automated survey at the time of their baseline/acceptability interview conducted as part of the parent study (study procedure #16)
23. At 12 weeks post discharge a research assistant will call participants to administer the last set of surveys as well as an acceptability questionnaire on the use of automated surveys to collect patient reported outcome measures (PROMS) (Appendix 17). Up to 5 attempts will be made to research participants for the survey at these time points.

Table 3: Survey administration timeline

	Day after discharge	2 weeks post discharge	4 weeks post discharge	6 weeks post discharge	12 weeks post discharge
Mobility survey	**x**	**x**	**x**	**x**	**x**
Financial Survey				**x**	**x**
General Survey				**x**	**x**
EPDS				**x**	**x**
Acceptability Survey				**x**	**x**

Biostatistical Analysis

Aim 1: The primary outcome measure is the rate of severe maternal outcome (SMO). This is a composite measure drawn from WHO near miss morbidity criteria (Table 2). Secondary outcome measures include: the maternal mortality rate, maternal near miss rate and case fatality rates for postpartum hemorrhage, hypertensive disease and sepsis – the three most common causes of maternal death. The event rates for both primary and secondary outcomes will be compared using logistic regression models with the Generalized Estimating Equations approach to take into account of patients within clustering (due to time blocks). Exploratory analyses will be used to determine if a) the intervention is more powerful in certain subgroups of women and b) if any provider was consistently different in maternal outcomes regardless of intervention. The interaction between study arm and comorbidities (HIV, hypertension, pulmonary, cardiac or kidney disease, malaria) or provider will be tested in the logistic regression models. Subgroup effects will be reported if there is strong evidence of heterogeneity of intervention effect

Aim 2: We will apply the RE-AIM model to conduct a quantitative evaluation of the implementation of the intervention used in Aim. Table 4 describes the primary metrics to be measured and data sources from which it will be collected.

RE-AIM Implementation Science Framework[37,38]			
Metric	**Dimension**	**Study Measure**	**Data source**
Reach	Proportion of target population that participated in the intervention	• Percent of women with successful placement of biosensor after delivery • Total length of time for monitoring over 24hrs postpartum • Percent of women participating in monitoring for 24 hrs	• Physiologic data from biosensor • Time of delivery from chart records & theatre log books
Efficacy	Success rate if implemented as in guidelines	• Percent of women with HR, BP, RR and Tp available at least every 4 hours for 24 hrs after delivery • Percent of appropriate SMS alerts sent	• Physiologic data from biosensor • RA review of mobile phones for SMS alerts and time of receipt
Adoption	Proportion of practitioners adopting this intervention	• Percent of clinicians participating in wireless monitoring • No. of clinical actions in response to SMS alerts	• RA review of medical record • RA review of mobile phones and medical record
Implementation	Extent to which the intervention is implemented in the real world	• Fidelity of implementation to the training protocol	• Documentations of any necessary adjustment to the protocol after study enrollment begins
Maintenance	Sustainability of program is over time	• Sustainability of reach, efficacy and adoption as measured by stability over measures over study period	• Above sources reviewed over time

The study measures for each of the 5 metrics will be compared by provider. Exploratory analyses will be used to determine if metrics are different by provider age, gender, years in clinical practice, and if timing of use (e.g. day vs night, week vs weekend) impacts implementation.

Aim 3: All qualitative data will be analyzed using standard qualitative methodologies. Specifically, data will be analyzed using content analysis, in an iterative, multi-step process.[39,40] We will review transcripts for key concepts used to develop a codebook, which will be used to code the data using software (NVivo) and to develop descriptive categories. Descriptive categories will be compared to the technology acceptance model as a framework for interpretation and used to qualitatively understand clinical adoption as measured in Aim 2

Aim 4 & 5: Through activity-based costing and time-tracking, we will estimate the costs of all observed activities. This micro-costing data will be used to estimate the average cost and effort of wireless monitoring a postpartum woman for 24 hours. Cost data will be estimated using Uganda Ministry of Health cost data where possible and other research cost inputs if necessary. Using the estimates of cost, we will combine this with outcome data from Aim 1 to estimate the cost-effectiveness of wireless monitoring for reducing SMO in postpartum women.

Aim 6: From the QUIC scale two scores are calculated: 1) the Informed Consent Aggregate Score (ICAS) and 2) the Therapeutic Misconception Aggregate Score (TMAS). ICAS assesses the quality of consent, ranging from 0-10 (10 is a perfect score) and TMAS assesses the presence of a therapeutic misconception (TMAS), ranging from 0-5 (5 is a perfect score). The ICAS and TMAS scores will be calculated and the means and standard deviations summarized for all participants. We will also summarize individual questions to understand the quality of specific elements of informed consent process. We will compare ICAS and TMAS between women in different stages of labor using one-way ANOVA, and with different pain scores using Spearman correlation and linear regression. Multiple

linear regression will be used to assess the independent association of covariates of interest (demographics, stage of labor, pain score, anxiety, obstetric history and trust) with ICAS and TMAS scores.

Aim 7: Using the motion metric on the wireless device we will summarize mobility in the first 24 hours after their cesarean both as a continuous variable ,and categorizing women into those with low and high mobility. We will summarize the functional status of women in the post discharge period according to the five dimensions measured by the mobility survey : (ability to move independently, ability to selfcare, ability to perform usual activities, level of energy, and overall health, as well as a compositive variable with scores of 1-4. 1 being poorest functional status and 4 being better functional status) We will describe functionality at the different time points after discharge using frequency and percent. We will compare return to functionality at the different time points by mobility category in the first 24 hours using regression modelling. We will also describe the rates of impoverishing and catastrophic expenditure after surgery. Summary statistics will be calculated for all expense types. We will compare impoverishing and catastrophic expenditure rates between women with different functional status and early mobility.

Sample Size:
On average approximately 8-10 emergency cesarean deliveries are performed at MRRH daily. Thus, in a two week block we estimate ~ 112 emergency cesareans performed. We plan to capture all women delivered by emergency cesarean during an intervention block thus minimizing the risk of selection bias based on the severity level. Assuming 85% of women consent to participation (conservative estimate based on >90% recruitment in prior studies)[5,74,75], this yields an estimated 95 women per block. Over 12 months of enrollment, we will therefore have 13 intervention blocks and 13 control blocks. This yields an estimated 1,235 women in the intervention group and 1,235 in the control group. Assuming an intraclass correlation coefficient of 0.01, the effective sample size after taking account of clustering is 633 per group. This will allow us to detect a difference of 5.7% in the SMO rate between the two study arms, with a two-sided significance level of 0.05, and 80% power, assuming a baseline rate of SMO of 13% [71,73]

Risk/Discomforts and protections
Clinicians:

- Risk of false alerts, alert fatigue: Clinicians will be asked to hold a mobile phone and respond to alerts. It is possible that alerts of physiologic sign abnormalities may not correspond to a developing or established clinical abnormality and in responding to the alert clinicians may become fatigued from alerts. Study investigators will monitor for this occurrence and the impact on clinician performance and duties and adjust study protocols as necessary
- Risk of diversion and interruptions to work on other patients: Alerts sent to clinicians may also prompt them to perform additional exams or clinical procedures that may or may not be beneficial to the patients from which alerts were received. This may divert attention or human resource away from other clinical needs. We will monitor for any diversions resulting in substandard clinical care. If these occur we will consider protocol modifications. Any safety concerns or adverse events arising because of false alerts or diversions will be communicated to the IRB within 10 days.

Peritpartum women:

- Theoretical risk of exposure to radio emissions from Wi-Fi from the biosensor: There is a theoretical risk of exposure to Wi-Fi signals from the biosensor worn by women participating in

the study. The FDA has indicated the majority of studies dealing with radio emissions from devices, such as mobile phones, have failed to show an association between exposure to radiofrequency from a cell phone and health problem. Regulatory bodies in both the United States and Canada have set Specific Absorption Rates (SAR) of <1.6 watts per kilogram, for radio emitting devices such as Bluetooth devices and cell phones sold in the United States. The SAR indicates the rate at which energy is absorbed when exposed to radio frequency. Mobile phones in the United States transmit in the range of 0.25 watts per kilogram when used near the ear. Bluetooth devices transmit a SAR of 0.001 watts per kilogram. Based on this data, Radiofrequency emissions from the biosensor are significantly lower than cell phone transmissions (Federal Communications Commission, "OET Bulletin 56: Questions and Answers about Biological Effects and Potential Hazards of Radiofrequency Electromagnetic Fields," www.fcc.gov, Aug. 1999). Moreover the biosensor and monitoring system to be used in this research protocol has been tested MRRH and approved for general use by the FDA

- Mild discomfort/skin irritation from wearing the device: The biosensor to be used is attached to the sternum using standard adhesives for electrode applications which have been approved and are in routine clinical use. In preliminary work women reported high acceptability related to the comfort of the device[18,31]; however, this study will require women to wear a different device and for a longer period of time and during a phase were breastfeeding is likely to occur. To minimize this risk, potential participants with known allergies or hypersensitivity to device materials will be excluded from the study. In addition, we will actively monitor for safety concerns (e.g. skin irritation, physical discomfort, disruptions to breastfeeding, and emotional concern with the monitoring) throughout the above described procedures through observation of the participants. We will review all reports of safety concerns within 24 hours and communicate any adverse events to the IRB within 10 days. The study team will also facilitate referral for any necessary medical care. If any adverse events are deemed related to the biosensor device, the study will be stopped until the safety issue is resolved.
- Risk of additional clinical interventions or exams that may or may not be beneficial: Alerts of abnormal physiologic signs may prompt doctors to perform additional exams and clinical interventions. If abnormalities in physiologic signs do not correspond to developing or established clinical abnormalities this may mean additional procedures are performed without benefit. We will monitor for any substandard clinical care to participants, or participant distress caused by this and modify study protocols as necessary.
- *Less than 24 hours between recruitment and consent:* As noted above peripartum woman will be approached for recruitment into the study once admitted to the unit for delivery to allow monitoring to begin immediately after delivery. Due to this timeline, there will be less than 24 hours between initial approach and consent. Particularly given the high intensity time around childbirth, this exposes the women to some vulnerability in decision-making. The RA recruiting and seeking consent will be carefully trained to fully explain the risks and benefits and to ensure women understand that they will still receive current standard of care at the hospital should they decline to participate. Women indicating interest in participating will be approached again once the decision has been made for an emergency cesarean delivery. Due to potential unpredictable changes in clinical course and the development of complications that may render a woman unable to provide consent for herself, we have limited enrolment to those women who can either consent for themselves or who have a guardian available to consent for themselves. Consent via a guardian is included as monitoring critically ill women who may be unable to provide their own consent is paramount to ultimately affecting clinical outcomes

Both clinicians and peripartum women:

- Stress and anxiety related to study procedures: Post-graduate doctors may experience some stress and anxiety due to the requirement to hold the responder phone particularly given they

will have other clinical responsibilities at the same time e.g. performing other procedures and evaluating other patients. Study investigators will actively monitor for impact on clinicians. We will review all reports of safety concerns within 24 hours and communicate any adverse events to the IRB within 10 days. 2)Any woman undergoing childbirth can have high levels of physical and emotional stress. Research participation during process may increase this stress and anxiety. During recruitment of both doctors and women it will be emphasized that participation is voluntary, and they are free to decline to participate or drop out at any point without repercussion.

- Risk of fatigue from interviewing: In depth interviews will be designed to take less than one hour. However, this time frame may induce fatigue in participants. We will ensure interviews last no more than one hour, and the qualitative RA is trained to take regular breaks as needed. Participants will be informed in advance that they can take a break or stop at any time. As there are two types of qualitative interviews, we will ensure that no one participant has to participate in more than one interview.
- Loss of privacy and confidentiality: Participants in all studies are subject to loss of privacy and confidentiality. In particular, physiologic sign data from postpartum women will be transferred to a central CPU or tablet for display and review by clinicians and abnormalities in physiologic signs sent a responder phone. In addition, medical information extracted from charts could be subject to loss of privacy. To ensure confidentiality all data will be maintained on password-protected, encrypted computers (if electronic) and/or locked cabinet (if hardcopy). All interviews will be held in a private location at a time convenient to the interviewee. All data, other than physiologic sign data for clinician review, will be coded by subject number. All RAs and interviewers will receive training on procedures for maintaining privacy.

Potential Benefits

Doctors will benefit from having easier and more timely access to physiologic data, reducing their work burden and improving their ability to more fully care for their patients. Postpartum women will have the direct benefit of increased physiologic monitoring. In some cases, this can be life-saving as developing complications may be averted from earlier intervention. In addition, I anticipate that wireless maternal monitoring will ultimately help reduce rates of maternal and newborn morbidity and mortality, particularly in resource-limited settings. The results of the proposed study will help establish the preliminary efficacy of this strategy for monitoring and how to improve implementation. Furthermore, understanding mobility in the postpartum period and the financial risks associated with childbirth and its recovery, may help us reduce these risks and improve recovery from cesarean deliveries. Both type of participants may feel good about contributing to research in this area.

Monitoring and Quality Assurance

Prior to conducting the study, the research assistants will receive training on how to use the data collection tool, as well as standard clinical research ethics (i.e., the online CITI course available through Massachusetts General Hospital [MGH]).

A member of the study staff will verify completion of data as entered into the chart review forms prior to data analysis. Missing or inconsistent data that can be verified with the participant's chart or interviewed clinician prior to discharge will be entered retrospectively. Data that cannot be verified with the participant or their chart will not be included in data analysis. All quality control measures will be performed on a weekly basis and as needed.

Qualitative data will be transcribed within 48 hours of data collection and then translated into English if need be.

The principal investigators shall provide oversight and review of study protocols throughout the study. Quality checks will be performed on a weekly basis by the principal and co-investigators to ensure accurate data collection.

The principal investigators will review all potential instances of privacy violations or other concerns within 24 hours and communicate any adverse events to the MUST and MGH IRBs within 10 days.

A Data and Safety Monitoring Board (DSMB) will be convened.

Our chosen DSMB will include the following

1. Dr. Josephat Byamugisha – Former Chair Dept of OB/GYN Makerere University
2. Dr. Sam Okello – Lecturer, Dept of Medicine, MUST
3. Dr. Bethany Hedt-Gauthier – Associate Professor of Global Health and Social Medicine, Biostatisticia, Harvard Medical School

The DSMB will meet 4 times during the anticipated 12-month study duration (prior to initiation, twice during the study, and at the end). Stopping rules will be discussed by the DSMB at the first meeting to establish criteria against which study progress and safety are measured at each further DSMB meeting. Specifically, we will ask the DSMB to review if there is a signal of higher rates of severe maternal outcome than expected to determine if these are related to the study intervention and then provide recommendations to study changes including but not limited to potential consideration of study termination. We will also ask their assistance in monitoring study implementation, including participant burden.

Additionally, we will convene a community advisory board who will review the planned study prior to it beginning and provide a resource for advice and recommendation should unexpected challenges arise during study implementation. We will again meet with the community advisory board to help disseminate the findings of our research to the community.