Early warning systems to improve maternal health in Nigeria: design, validation and evaluation of a modified obstetric early warning chart for use in low-resource settings

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by

Aminu Aliyu Umar

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Dedication

To my late mum, Jummai Chiroma, who would have been very proud

To Dad, AU Misau, for being the best dad in this world

To my wife, Dr Na'imah Mohammed, for her unwavering love and support

To Ahmad and Ummulkhair, for being the love of my life

To all those contributing towards better-quality maternal care around the world

Declaration

I, Aminu Umar, confirm that this thesis is the result of my work. Where information has been obtained from other sources, I confirm that this has been indicated in the thesis. The material contained has not been presented, nor is it currently being presented, either wholly or as part of any other degree, or other qualification.

Acronyms

ANC	Antenatal Care
ANOVA	Analysis of variance
AUROC	Area Under Receiver Operating Characteristic Curve
BEmOC	Basic Emergency Obstetric Care
CAQDAS	Computer-assisted Qualitative Data Analysis Software
CDC	Centre for Disease Control
CEMACH	Confidential Enquiry into Maternal and Child Health
CEmOC	Comprehensive Emergency Obstetric Care
CI	Confidence interval
CMNH	Centre for Maternal and Newborn Health
DHS	Demographic and Health Survey
EWS	Early Warning Systems
FGD	Focus Group Discussion
GDP	Gross Domestic Product
ICU	Intensive Care Unit
IMEWS	Irish Maternity Early Warning System
KII	Key Informant Interview
LMICs	Low and Middle-Income Countries
LSTM	Liverpool School of Tropical Medicine
MEWC	Maternal Early Warning Criteria
MEOWS	Modified Early Obstetric Warning System
MEWT	Maternal Early Warning Triggers
NEWS	National Early Warning System
NPMS	National Partnership for Maternal Safety
NPV	Negative Predictive Value
PPV	Positive Predictive Value
RANZCOG	Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RCOG	Royal College of Obstetricians and Gynaecologists
SASOG	South African Society of Obstetricians and Gynaecologists\
WHO	World Health Organization

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Abstract

Background: One basic way to prevent maternal deaths in healthcare facilities is through early detection of changes in physiological parameters that are suggestive of clinical deterioration before such changes become irreversible and fatal. This is the aim of the Early Warning Systems (EWS). The objectives of this PhD were to introduce and evaluate the use of obstetric EWS in Nigerian tertiary hospitals.

Methods: A preliminary investigation of the evidence supporting the usefulness of EWS in obstetric practice was achieved via a systematic literature review. The baseline formative research employed mainly qualitative methods to assess the feasibility of implementing EWS in three Nigerian tertiary hospitals. Then a robust dataset, consisting of 4360 women with severe maternal outcome (SMO: maternal death or near miss) and 1000 obstetric admissions without SMO diagnosis, collected across 42 Nigerian tertiary hospitals, was used to develop a statistically derived obstetric EWS model and score-based chart for use in low-resource settings using a case-control multivariate logistic regression analysis. The resulting EWS chart was implemented across all obstetric units of a university teaching hospital in Nigeria. Two other teaching hospitals were recruited as control facilities. Following implementation, we employed mixed research methods to assess the effectiveness of EWS in improving health outcomes and explore the experience of health workers/managers implementing the EWS.

Results: The systematic review showed that EWS are effective in predicting severe obstetric morbidity and mortality, can potentially contribute to improved quality of care/health outcomes, and may be feasible to implement in low-resource settings. The feasibility study confirmed the absence of EWS, a checklist or any guidelines on how to trigger response to obstetric emergencies across the three hospitals. Vital signs were routinely monitored despite shortages of monitoring equipment and human resources. However, understanding of their potential utility as early pointers to maternal deterioration was deficient among healthcare workers.
The resulting EWS from our SMO model consisted of seven clinical parameters (respiratory rate, temperature, systolic blood pressure, pulse rate, consciousness level, urine output and delivery mode for postpartum patients). The model had excellent screening characteristics for SMO (86% (95% CI 81–90) sensitive and 92% (95% CI 89–94) specific and maintained good discriminatory power across all our internal validation data sets (area under ROC curves consistently above 90%).
Following implementation, nurses and doctors found EWS easy to use, easy to evaluate at a glance, and accurate, but, usage rate was considerably low (<50%). Significant improvement in quality of vital signs monitoring was experienced in the intervention, but not in any of the control sites. Rotation of clinical staff, shortages of monitoring equipment and human resources for health were identified challenges.

Conclusion: To the best of our knowledge, this research reports for the first time an internally validated statistically developed diagnostic predictive model for obstetric morbidity and mortality among all women admitted to obstetric wards in a low-resource setting. Our findings showed that it is feasible to implement the obstetric EWS in low-resource settings and this can improve the quality of patient care through better monitoring frequency and medical review based on abnormally high EWS scores. The EWS we developed could be used to evaluate quality of patient care through assessing whether trigger events result in clinical action, and timeliness of clinical action. Surveillance of patients who trigger action could allow for further evaluation and discussion of quality of care, for example at maternal morbidity and mortality meetings.

Overall, with staff education on usefulness of EWS, coupled with continuous training and retraining, it is feasible to implement obstetric EWS as a potentially acceptable patient monitoring tool to cope with the unique demands faced by obstetric practice in low-resource tertiary healthcare settings.

Chapter 1: Introduction

1.1. Overview of the chapter

This introductory thesis chapter starts with a background of the global maternal health situation, particularly in low- and middle-income countries, and the focus of global strategies to improve maternal and newborn health outcomes during and after the Millennium Development Goals (MDGs) era. This chapter then introduces early warning systems (EWS) – what they are, the different types in use, their application in other non-obstetric clinical specialities, and the UK National Early Warning Scores (NEWS). Subsequently, it details the rationale for having modified EWS in the obstetric population and how these have evolved over time, leading to the rationale for this study. This chapter concludes with the aim and objectives of this research project and an overview of the remaining chapters.

1.2. Background

Global maternal mortality remains excessively high, with an estimated 303,000 women dying each year because of pregnancy and childbirth-related complications (WHO, 2015). Although there was a 44% decline in the worldwide maternal mortality ratio (MMR) – the number of maternal deaths per 100,000 live births – between 1990 and 2015, the recorded global success was far short of the 75% reduction that was required to achieve the maternal health target of the Millennium Development Goals (MDGs) (Alkema et al., 2016). At the end of the MDG era in 2015, 25 low- and middle-income countries (LMICs) still had an MMR of 420 per 100,000 live births or greater, with an estimated 80-fold higher lifetime risk of maternal mortality compared to high-income countries (Alkema et al., 2016). This points to maternal health inequality that must be addressed going forward.

The reasons for lack of steady progress across all countries, particularly in the low- and middle-income settings, are complex and multifactorial. Evidence from the *Lancet* series on maternal health identified poor quality of available care, inequalities in access to care, especially for vulnerable populations, and grave deficiencies in health system infrastructure and workforces as the key factors

impeding progress towards reduction of mortality and morbidity (Ceschia & Horton, 2016; Freedman, 2016; Graham et al., 2016; Koblinsky et al., 2016).

Over the past decade, global strategies to reduce adverse outcomes for pregnant women and newborns have focused on increasing skilled birth attendance (Secretary-General UN, 2010; Tunçalp et al., 2015; WHO, 2005). This has improved access to facility-based births in all regions, with the proportion of deliveries reportedly attended by skilled health personnel rising from 56% in 1990 to almost 80% by 2017 (United Nations, 2018). With the resulting increase in utilization of health services, a higher proportion of preventable maternal morbidity and mortality have moved from communities to health facilities. In view of this, poor quality of care in healthcare facilities has become a major bottleneck in the quest to end preventable maternal morbidity and mortality (Tunçalp et al., 2015).

To address the unfinished agenda of reducing maternal mortality in the post-MDG era, the WHO and partners conceptualized the *Strategies toward ending preventable maternal mortality (EPMM)*, which was launched in 2015 with a view to achieving equitable and high-quality coverage of care for all women and newborns (WHO, 2016a). This was a direction-setting initiative with both national and global targets and strategies, which were adopted by the Sustainable Development Goals (SDGs) framework for reducing preventable maternal mortality worldwide (Jolivet et al., 2018). The strategies are focused on the principles of equity and non-discrimination, transparency, participation and accountability, to ensure that high-quality reproductive, maternal and newborn healthcare is available, accessible and acceptable to all who need it (Jolivet et al., 2018).

The WHO vision of quality of care for pregnant women and newborns defines quality of care as *"the extent to which health care services provided to individuals and patient populations improve desired health outcomes"* (Tunçalp et al., 2015). Quality of care is a crucial component of the right to health, and the route to equity and dignity for women ("WHO | independent Expert Review Group (iERG)", 2015). This was further reiterated in the new Global Strategy for Women's, Children's and Adolescents' Health (2016–2030), which targets multiple dimensions of quality of care to reduce the burden not just of preventable maternal mortality, but also of

severe morbidity in the post-2015 SDGs era (United Nations, 2015b). Such a global vision cannot be achieved without a focus on timely identification and treatment of major obstetric complications (mainly haemorrhage, hypertensive disorders and sepsis), which account for more than 70% of maternal deaths occurring worldwide (Say et al., 2014b), yet are often identified and treated too late.

1.3. Early warning systems (EWS)

Early warning systems, also known as physiological track and trigger systems, are clinical prediction models that involve serial clinical observations (track) to identify a pattern that is consistent with increased risk of deterioration and alert (trigger) health workers to intervene to improve outcomes (Gao et al., 2007; Goldhill, et al, 2005). These systems are predicated on the idea that derangement in simple physiological observations can identify hospitalized patients at high risk of deterioration (Goldhill & McNarry, 2004). They assign weighted values to these physiological observations (such as respiratory rate, temperature, pulse rate and blood pressure) based on their degree of deviation from normal and define pathophysiological thresholds beyond which mandatory actions must be taken to prevent irreversible morbidity or death (Gao et al., 2007).

1.4. EWS in non-obstetric specialities

EWS have been used in other non-obstetric specialities since 1997 (Morgan & Williams, 1997). Several types of EWS have been described (Patterson et al., 2011). These range from single-parameter to multi-parameter or aggregate weighed scoring systems. The single-parameter EWS define abnormal pathophysiological trigger thresholds for a list of patient monitoring physiological parameters (such as blood pressure), and bedside medical evaluation (trigger) is indicated when any single EWS parameter is measured as abnormal. On the other hand, aggregate weighted scoring systems are multi-parameter EWS tools in which a score is assigned based on degree of deviation from normal for each measured physiological parameter; a clinical staff member undertaking patient monitoring (often a nurse or midwife) or a computer algorithm calculates the cumulative (EWS) score based on inputs for all parameters (Zuckerwise & Lipkind, 2017). This cumulative score is used to determine the likelihood of deterioration and the need for bedside medical evaluation.

In general, aggregate weighted scoring systems have proved more sensitive than single-parameter EWS (Zuckerwise & Lipkind, 2017). Various non-obstetric EWS versions have been proved to successfully identify inpatients at highest risk of severe morbidity (such as cardiac arrest or ICU admission) and mortality in general medical, surgical and intensive care patients (Piper et al., 2014; Smith et al., 2014; Subbe, et al, 2001). In a systematic review of non-obstetric EWS for adults admitted to medical and surgical wards, Smith and colleagues reviewed 21 papers including data on 13 distinct EWS, and reported an excellent ability to predict patients at highest risk of death or cardiac arrest within 48 hours, with an area under the receiver operating characteristic (ROC) curve of 0.88–0.99 and 0.74–0.86 for death and cardiac arrest, respectively, for all studies/models included (Smith et al., 2014).

As with the adult systems, the paediatric EWS created by Duncan and colleagues to predict actual or impending cardiopulmonary arrest in hospitalized children has been shown to be 78% sensitive and 95% specific in predicting actual or impending cardiopulmonary arrest, with an area under the ROC curve of 0.9 (Duncan, et al, 2006).

1.5. National Early Warning Score (NEWS)

The number of non-obstetric adult EWS proliferated following their inception in 1997, but the quality of data supporting the use of individual systems has been described as generally poor (Friedman, 2015). Additionally, lack of consistency in detecting deterioration of patients' conditions by the various available EWS versions used in United Kingdom (UK) hospitals was the major concern, which led the Royal College of Physicians to design a standard national EWS for the non-obstetric adult patient population in the UK. This is called the National Early Warning Score (NEWS, **Table 1**) (Friedman, 2015).

NEWS was first produced in 2012 and updated in December 2017. Specifically, it was designed to address the challenges created by the proliferation of different non-obstetric EWS including 1) varying parameters and weighting leading to unfamiliarity across hospitals or in different clinical settings within hospitals, 2) poor validation of EWS in detecting a broad range of acute severe illness across different clinical settings, 3) lack of clear definitions for an appropriate clinical response in

the setting of a positive alert, and 4) an absence of uniform criteria to base undergraduate and postgraduate training ("National Early Warning Score (NEWS) 2 | RCP London", 2017) (Friedman, 2015). The NEWS parameters and scoring system are shown in **Table 1.1**.

Table 1 1 The NEWS scoring system

Physiologic Parameters	**3**	**2**	**1**	**0**	**1**	**2**	**3**
Respiratory rate/ min	≤8		9-11	12-20		21-24	≥25
SpO2 Scale 1* (%)	≤91	92–93	94–95	≥96			
SpO2 Scale 2* (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic BP (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse rate	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			*VPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

Scale 1: for patients with normal respiratory function; scale 2: for patients with obstructive pulmonary disease (COPD with target SPO2 88-92%): VPU; responsive to voice, pain or unresponsive
Available at https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2. Accessed January 10, 2019; reproduced with permission.

Six simple physiological parameters form the basis of the scoring system: respiration rate (breaths per minute), oxygen saturation (%), systolic blood pressure (mm Hg), pulse rate (beats per minute) and temperature (degrees Celsius). Level of consciousness is based on the Alert, Voice, Pain, Unresponsive (AVPU) scale, which assesses four possible outcomes to measure and record a patient's level of consciousness. A score is allocated to each parameter as it is measured, with the magnitude of the score reflecting to what extent the parameter varies from the norm. The score is then aggregated and uplifted by two points for people requiring supplemental oxygen to maintain their recommended oxygen saturation ("National Early Warning Score (NEWS) 2 | RCP London", 2017).

A low score (NEWS of 1–4) should prompt an assessment by a registered nurse. A medium score (NEWS of 5–6) should prompt an urgent review by a doctor or team with competence in the assessment and treatment of acutely ill patients and in recognizing when the escalation of care to a critical care team is appropriate. A high

score (NEWS of 7 or more) should prompt emergency assessment by a critical care team (to include staff with airway management skills) with likely transfer of patient to a higher acuity team ("National Early Warning Score (NEWS) 2 | RCP London", 2017).

During its development, the NEWS was evaluated against a variety of other EWS in use and was shown to be as good at identifying risk of serious clinical deterioration and acute mortality as the best existing systems and better than most in use ("National Early Warning Score (NEWS) 2 | RCP London", 2017; Smith, et al, 2014). Furthermore, at the recommended trigger level for an urgent clinical response (NEWS score of 5 or more), the NEWS was more sensitive and specific than most existing systems (Smith et al., 2014). Thus, the NEWS provided an enhanced level of surveillance of patients, with greater specificity in identifying those at risk of serious clinical deterioration. Subsequent experience in the use of NEWS in clinical practice and formal research-based evaluations has reaffirmed that the NEWS performs very well ("National Early Warning Score (NEWS) 2 | RCP London", 2017).

1.6. Applicability of NEWS and other adult EWS to obstetrics

Several versions of adult EWS (especially the NEWS) have been validated in many settings within the UK NHS and internationally, including emergency departments and in the prehospital care setting, i.e., by ambulance services (Farenden, et al, 2017; Jarvis et al., 2015; Silcock, et al, 2015; Smith et al., 2016). In these studies, EWS have been shown to be strong indicators of increased risk of serious clinical deterioration and mortality in patients with sepsis and a variety of acute medical illnesses, surgical patients, and patients with acute trauma. Unfortunately, however, these EWS have failed to prove useful in obstetric patients, as the evaluation and triggering criteria that underlie their development do not account for the physiological changes of pregnancy (Lappen, 2010).

Since small changes in thresholds can make substantial differences to the ability of clinical scores to identify physiological deterioration, accurate reference ranges that take into account the physiological changes of pregnancy are essential to using EWS to provide high-quality clinical care to obstetric patients (Smith, et al, 2008).

Considering this, and in response to the increasing maternal morbidity and mortality burden, there has been a concerted effort to define a viable EWS for the obstetric population (Zuckerwise & Lipkind, 2017).

In 2007, the Confidential Enquiry into Maternal and Child Health (CEMACH) report published data from 2003–2005 in the UK indicating that in many cases of severe maternal morbidity and mortality there was a failure to recognize signs of impending maternal collapse. This report recommended routine use of an early warning chart specially adapted for the obstetric population, called the modified early obstetric warning system (MEOWS) (**Annex 1A**), with plans to evaluate and pilot this as a national obstetric EWS (Cantwell et al., 2011).

> *"...there is an urgent need for the routine use of a national obstetric early warning chart, similar to those in use in other areas of clinical practice, which can be used for all obstetric women which will help in the more timely recognition, treatment and referral of women who have, or are developing a critical illness* (CEMACH, 2007)*…"*

1.7. Modified early obstetric warning system (MEOWS)

The MEOWS was proposed by the UK CEMACH (CEMACH, 2007). The tool development was undertaken by highly informed experts who agreed by consensus on the inclusion of parameters in the chart, and pathophysiological cut-off (trigger) points. The resulting MEOWS tool has 12 clinical parameters (**Annex 1A**): these are measurements of temperature (oral), heart rate, blood pressure, respiratory rate, oxygen saturation (pulse oximeter), consciousness level (based on AVPU), general condition (looks unwell), passage of urine (yes or no), proteinuria (urine dipstick test), colour of amniotic fluid, colour of lochia and pain score. The reference ranges and trigger cut-off points of the MEOWS variables are illustrated in **Table 1.2**.

Table 1 2 MEOWS variables: normal ranges and trigger criteria (CEMACH 2007)

Variable	Normal range or pregnancy	Yellow (caution) trigger	red (urgent) trigger
Respiratory rate (breaths/min)	10-20	21-30	<10 or >30
Temperature (Celsius)	37-38	35-36	<35 or >38
Heart rate (beats/min)	51-99	40-50 or 100-120	<40 or >120
Systolic BP (mmHg)	101-149	90-100 or 150-160	<90 or >160
Diastolic BP (mmHg)	<80	80-90	>90
Oxygen saturation (%)	>90	No trigger	<90
Looks unwell	No	Yes	No trigger
Neurologic response	Fully responsive	Responsive to voice	To only pain, unresponsive
*Pain score	0-1	2-3	No trigger
Amniotic fluid	Clear	No trigger	Green
Lochia	Light-moderate, no odour	No trigger	Heavy or foul
Passed urine (yes/no)	Yes	No trigger	No trigger
Dipstick proteinuria	Negative, trace	No trigger	>2+

*The "pain score" assesses pain on movement, deep breathing, or coughing as follows: 0 for no pain at rest or on movement, 1 for no pain at rest but slight pain on movement, 2 for intermittent pain at rest and moderate pain on movement, and 3 for intermittent pain at rest and moderate pain on movement.

A MEOWS trigger is defined as a single markedly abnormal observation (red trigger) or a combination of two simultaneously occurring mildly abnormal observations (two yellow triggers, **Table 1.2**). The MEOWS parameters, which are routine clinical observations, are recorded on the chart on admission to the hospital. Subsequently, according to the two MEOWS validation studies (Singh, A et al, 2016; Singh S et al, 2012), the parameters are monitored based on the following frequencies for different categories of obstetric patients: 1) for women in labour: four-hourly until 24 hours after delivery, and then daily until discharge; 2) haemorrhage and other obstetric complications: every hour for four hours, then four-hourly for the next 24 hours and thereafter once a day until discharge; 3) caesarean section or other procedures under anaesthesia: every hour for six hours, then four-hourly for the next 48 hours and then once a day until discharge; and 4) blood transfusion: immediately prior to start of transfusion and then 15 minutes into the transfusion.

1.8. MEOWS and partograph

The partograph is a graphic recording of progress of labor and salient conditions of the mother and fetus plotted against time in hours, hence unlike the MEOWS, it is used in labouring women only. In 1954, Friedman started the concept by depicting the cervical dilatation during labour in an S-shaped curve, which was modified by Philpott and Castle in 1972, into a tool for monitoring of labour by adding 'Action

and Alert' lines, and later modified and adopted by the WHO in 1988 and recommended for worldwide use in all healthcare settings. (Friedman EA, et al, 1954; Philpott RH & Castle WM 1972).

The aim of the partogram/partograph is to provide a pictorial overview of labour, to alert healthcare providers to deviations in maternal or fetal wellbeing. By mapping the cervical dilatation against time, unsatisfactory progress of labour can be identified and managed promptly. The alert and action lines are pre-printed. An alert line represents the slowest 10% of primigravid women's labour progress. An action line is placed a few hours after the alert line (usually two or four hours) to prompt effective management of slow progress of labour (Lavender et al, 2013). Such practice is also recommended by the World Health Organisation (WHO) for use in active labour (Penumadu et al, 2014).

Structurally, the main difference between partograph and MEOWS chart is that the latter focusses solely on maternal monitoring, while partograph has both maternal and fetal clinical parameters. The clinical value of both tools depends on accurate observations, correct completion, and effective application of findings for effective clinical decision-making. The partograph therefore has a trigger that is the alert line; its efficiency will depend on accurate clinical examination, correct completion of the partograph and correct interpretation. If these are inaccurate there is a risk of increased interventions such as caesarean sections.

1.9. Evolution of obstetric EWS

Following the CEMACH recommendation of MEOWS, there was widespread adoption among hospitals and maternity units in the UK, with varying degrees of modification of parameters and trigger thresholds, but none was adopted as the gold standard (Smith et al., 2017). In 2014, a survey of obstetric anaesthesiologists around the UK was designed to assess the responsiveness to the CEMACH recommendation (Isaacs et al., 2014); the results indicated high compliance, with 100% (n =130) of respondents replying affirmatively to obstetric EWS use. While the actual EWS in use varied between the study sites, there was general agreement on the parameters to be included. Temperature, heart rate, respiratory rate and systolic blood pressure appeared on 100% of the EWS in use (Isaacs et al., 2014;

Smith et al., 2017). Additional common parameters included oxygen saturation (98%), diastolic blood pressure (95%) and urine output (85%). Importantly, 91% of respondents agreed that their EWS could help prevent maternal morbidity (Isaacs et al., 2014).

Similar to the UK CEMACH, the United States National Partnership for Maternal Safety (NPMS) aims to reduce preventable maternal morbidity and mortality by identifying and addressing opportunities to improve maternal safety (Mhyre et al., 2014). In order to facilitate timely diagnosis and treatment for women developing critical illness, the Subcommittee on Vital Sign Triggers sought to ascertain tested examples of obstetric warning systems, define considerations for local implementation, and organize lists of differential diagnoses to facilitate timely and accurate diagnosis (Mhyre et al., 2014). Using a consensus-based approach, this multidisciplinary working group developed a single-parameter early warning scoring system, the maternal early warning criteria (MEWC, **Table 3**), and recommended its use in antepartum, intrapartum and post-partum settings throughout the United States (Mhyre et al., 2014).

Table 1 3 Maternal early warning criteria (MEWC)

Variable	Trigger
Systolic BP (mmHg)	<90 or >160
Diastolic BP (mmHg)	>100
Heart rate (beats/min)	<50 or >120
Respiratory rate (breaths/min)	<10 or >30
Oxygen saturation (%), on room air, at sea level (%)	<95
Oliguria, mL/hr for >2 hours	<35
Maternal agitation, confusion or unresponsiveness; Patient with pre-eclampsia reporting a non-remitting headache or shortness of breath	

These triggers cannot address every possible clinical scenario that could be faced by an obstetric clinician and must not replace clinical judgement. As a core safety principle, bedside nurses should always feel comfortable to escalate their concerns at any point: Source (Mhyre et al., 2014).

The MEWC was developed from MEOWS red triggers; temperature was deleted from the criteria given the panel's impression that fever is commonly accompanied by other vital signs derangements and is unlikely to be missed or dismissed in routine clinical care. Pain was removed because of its established poor relationship with severe maternal morbidity (Mhyre et al., 2014; Singh S et al, 2012). On the other hand, a measure of low urine output (oliguria) was included, given its importance as a sign of clinical progression for women with severe pre-eclampsia; however, quantitative monitoring of urine output is only indicated for women with a clear clinical indication (for instance, women having pre-eclampsia with severe features, major abdominal surgery in the immediate perioperative period, presence of suspected haemorrhage or sepsis). The cut-off point for bradycardia was raised from 40 beats per minute to 50 beats per minute. Also, an increasing requirement for supplemental oxygen to maintain a normal oxygen saturation was included as a substitute for absolute oxygen saturation as this appears to be a more specific measure of respiratory deterioration (Carle et al, 2013; Mhyre et al., 2014). Finally, consciousness level/critical neurological signs were expanded to include agitation, confusion, and unrelenting headache in the presence of hypertension (Mhyre et al., 2014).

The frequency of vital signs monitoring using MEWC is based on the woman's medical and obstetric condition, and in accordance with hospital-specific clinical guidelines (Mhyre et al., 2014b). Prompt bedside review by a physician or other clinical staff is indicated for all women who meet any of the MEWC, in order to

initiate emergency diagnostic and therapeutic interventions as needed. MEWC was presented at the annual clinical meeting of the American College of Obstetricians and Gynaecologists in May 2013, after which the American Congress of Obstetricians and Gynaecologists District II's Safe Motherhood initiative, a collaboration to improve maternal outcomes in New York, endorsed the tool for use in all hospitals providing obstetric services (Mhyre et al., 2014; Zuckerwise & Lipkind, 2017).

A similar effort to that of NPMS was made by a large hospital group consisting of 29 hospitals providing tertiary maternity services in the United States, which designed a preliminary study to test their obstetric EWS, the maternal early warning triggers (MEWTs, **Table 4**) (Hedriana, et al, 2016).

Table 1 4 Maternal early warning triggers (MEWTs)

Variable	Trigger
Temperature	≥38 or ≤36
Systolic BP (mmHg)	<80 or >155
Diastolic BP (mmHg)	>105 or <45
Mean arterial BP (mmHg)	Severe <50
Heart rate (beats/min)	<50 or >110
Respiratory rate (breaths/min)	<12 or >24 Severe >30
Oxygen saturation (%)	<90
Neurological assessment	Altered mental status
Fetal heart rate (beats/min)	>160

Like MEWC, the MEWTs are a single-parameter EWS consisting of a list of vital signs thresholds, as well as altered mental status (**Table 4**). A retrospective case-control study comparing the presence of MEWTs between obstetric patients admitted into the ICU and control obstetric patients with uncomplicated births reported that two or more MEWTs occurred more frequently in ICU patients. More importantly, the authors found that presence of persistent MEWTs (lasting at least 30 minutes) further delineated the ICU population from the controls (Shields et al, 2016).

Unlike the two popular EWS (MEOWS and MEWC), the MEWTs contained a flow diagram in addition to the trigger system, which functioned as a pathway-specific tool, designed to guide evaluation and emergent management of the four most common causes of severe maternal morbidity and mortality (haemorrhage, sepsis, cardiopulmonary dysfunction, and pre-eclampsia/hypertension). Over a 13-month

study period following implementation of MEWTs, the authors noted a significant reduction in CDC-defined severe maternal morbidity and composite maternal morbidity in the study sites (Hedriana et al., 2016; Shields et al, 2016). The authors reported good adherence to their study protocol, and wide acceptance of the monitoring tool among the hospital's clinical staff, as a positive screen resulted in physician intervention within 60 minutes in 82.3% of cases; hence, MEWT implementation was reported as a huge success (Shields et al, 2016).

Using the three major obstetric EWS types discussed above as bases, several charts were derived and adopted by hospitals and maternities internationally, with varying modification of the parameters and trigger thresholds (Smith et al., 2017). As with the three charts, most of these EWS versions were designed by clinical consensus rather than by application of recommended prediction model development methodology, which includes statistical analysis of outcome measures (Austin et al., 2014; Edwards et al., 2015; Shields et al., 2016; Smith et al., 2017). Model development involves statistical combination of predictor clinical observations into a multivariable model. The Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement recommends that new prediction models are tested on data used in its development (internal validation) and other data not used (external validation) (Collins et al, 2015).

In 2013, the first statistically derived obstetric EWS was developed and internally validated in the UK using clinical observations (physiological variables) collected from 4400 women admitted to critical care units from 1995 to 2008 (Carle et al., 2013). Physiological variables collected during the first 24 hours of critical care admission were analysed. Logistic regression analysis for mortality in the model development set was initially used to create a statistically based EWS. The statistical score was then modified to create a clinically acceptable EWS. The most distinct feature of the derived clinical obstetric early warning score is that the variables were weighted according to their statistical importance. The resulting EWS with nine clinical parameters (**Table 5**) showed a good predictive ability to discriminate survivors from non-survivors in the derivation data set (Carle et al., 2013), and on an external data set consisting of 702 women admitted to intensive care units (ICU)

(Paternina-Caicedo et al., 2017). The areas under the ROC curves were 0.957 (95% confidence interval (CI), 0.923–0.991) in the derivation data set and 0.87 (95% CI, 0.79 to 0.95) in the external data set.

Table 1 5 Statistically derived clinically modified obstetric EWS chart

Physiological Parameters	3	2	1	0	1	2	3
Systolic BP (mmHg)	≤80	80–89		90–139	140–149	150–159	≥160
Diastolic BP (mmHg)				<90	90–99	100–109	≥110
Respiratory rate (per minute)	<10			10–17	18-24	25–29	≥30
Heart rate (per minute)	≤60		60–110	51–90		111–149	≥150
%O2 required to maintain SPO2≥96%				room air	24–39		≥40
Consciousness level				Alert			Not alert
Temperature (°C)	<34.0		34.0–35.0	35.1–37.9	38.0–38.9		≥39

Urine output, pain score, FIO2 and SpO2 recorded elsewhere on chart. Alert*, alert and orientated, equivalent to Glasgow Coma Score (GCS) 15 and A on the Alert/Voice/Pain/Unresponsive (AVPU) scale; Not alert*, GCS 3–14 or V, P, U on the AVPU scale. Source Carle et al. (2013a).

However, since the database used in the development, internal (Carle et al., 2013a) and external (Paternina-Caicedo et al., 2017) validation of the EWS was only for women admitted to critical care, the EWS may not be suitable for obstetric patients without obvious need for critical care and other settings.

1.10. Rationale for the study

Despite the progress made globally in maternal health, there still remains a high burden of maternal morbidity and mortality in less developed countries of the world, most of which made insufficient progress towards achieving the MDG maternal health targets (Alkema, 2016). Working towards achieving even more ambitious SDG MMR targets would require implementation of key strategies to improve quality of maternal and newborn health services (United Nations, 2019).

Several strategies have been explored to improve access to quality maternity services, with variable success, but overall these have not resulted in the expected reductions in maternal mortality and morbidity, especially in low-resourced

countries, which have 14 times higher maternal mortality rates when compared to rates in developed regions (Alkema et al., 2016). This underscores the need to explore innovative approaches that could potentially improve the quality of care and reduce the risk of maternal mortality, especially in these settings.

One of the proposed strategies to improve quality of care is the use of obstetric EWS to aid timely identification and management of obstetric complications (CEMACH, 2007; Friedman et al., 2018; Mhyre et al., 2014). To the best of our knowledge at the time of conceptualizing this study, there was no up-to-date synthesis of evidence on overall effectiveness of EWS in the obstetric population. However, emerging evidence from several validation studies has reported the usefulness of obstetric EWS as screening tools for obstetric morbidity, with the potential to reduce the burden of maternal deaths and associated long-term complications (Friedman et al, 2018; Paternina-Caicedo et al., 2017; Singh A et al, 2016; Singh S et al, 2012; Zuckerwise & Lipkind, 2017). Given the evolving evidence, the 2017 Society for Maternal-Fetal Medicine's (SMFM) annual meeting dedicated a session to exploring early warning systems implementation across a wide range of hospital settings (Friedman et al., 2018). Among their top recommendations was that in order to effectively reduce maternal risk, EWS that capture deterioration from a broad range of conditions are necessary, in addition to bundles tailored to specific conditions such as haemorrhage, thromboembolism, and hypertension (Friedman et al., 2018).

Most importantly, a systematic review, conducted as part of this PhD project, provided an up-to-date synthesis on the evidence of effectiveness of obstetric EWS, and is presented in depth in **Chapter 2** (published output of this thesis (Umar, A., et al*.,* 2019). The findings from this review strongly support the usefulness of EWS both as triaging tools and in improving quality of care and measured patient outcomes. The review also provides evidence supporting the feasibility of use of EWS in low-resource settings with the potential to contribute to a reduction in maternal morbidity and mortality (Umar A et al*.,* 2019). However, despite being used in 100% of UK hospital maternity units (Isaacs et al., 2014) and several other

well-resourced countries, no obstetric EWS has been designed and validated for low-resource settings.

Finally, evidence from a prospective cohort study conducted in Malawi (Wheeler et al., 2013) showed that transferring an EWS generated in a developed healthcare setting into a resource-limited setting is likely to impact negatively on its performance, despite the assumption that physiological responses to diseases are common to all patients. Specifically, this resulted in a loss of both sensitivity and specificity of the adopted EWS tools, and a score based on predictors of mortality specific to the Malawian population showed much-enhanced accuracy (Wheeler et al., 2013). This underscores the need for local validation and impact assessment of EWS tools before their adoption in resource-limited settings.

It was therefore imperative to design and validate an obstetric EWS for use in low-resource settings with a view to improving the quality of care and reducing the overwhelming burden of maternal morbidity and mortality in these settings.

1.11. Aim and objectives

Aim

This research aimed to introduce and evaluate the use of obstetric early warning systems in Nigerian tertiary hospitals.

Objectives

1. To explore evidence on the overall usefulness of EWS in the obstetric population, and the feasibility of implementing them in low-resource settings, via a systematic review.
2. To conduct a baseline feasibility study using mixed research methods (quantitative and qualitative) in selected Nigerian tertiary care hospitals.
3. To develop and validate a simple obstetric early warning chart for use in resource-limited settings using recommended statistical methods.
4. To assess the effectiveness of the chart in improving measured patient outcomes through a prospective interventional study.
5. To explore the experience and challenges of using the chart among healthcare providers, using a qualitative research approach.

1.12. Structure of the thesis

To achieve the research goals, the project was structured in three phases, following a baseline systematic literature review to achieve the first research objective: 1) **phase 1** (feasibility study) to achieve the second objective; 2) **phase 2** (design and validation of obstetric EWS) to address the third objective; and 3) **phase 3**, comprising a controlled quasi-experimental trial and qualitative interviews/focus group discussions designed to achieve objectives 4 and 5 respectively. For the purpose of this thesis, I will be presenting the research in the next seven chapters as described below.

Chapter 2: Systematic literature review The objectives of this systematic review were 1) to synthesize the evidence on the effectiveness of obstetric EWS as screening tools for morbidity and mortality (predictive accuracy), and their usefulness in improving clinical outcomes in obstetric populations; and 2) to determine the evidence on the feasibility of implementing obstetric EWS in low-resource settings. The chapter starts with a brief rationale for the review, then covers the methods used to achieve the review's objectives. Critical appraisal/quality assessment of included studies is then discussed, and review findings are presented and discussed. Finally, the chapter ends with a summary of key points from the review and a conclusion of the synthesized evidence. This review was published in 2019 (Umar A et al., 2019) and the publication is included in **Annex 7**.

Chapter 3: Methodology This chapter gives an overview of the methodology used in the thesis. It defines key terms used in the research, describes the study settings in detail, and the study designs used, with rationale for choice of designs, and provides an overview of the data collection methods used. Thence, the chapter discusses overall considerations for ethics across all study phases and data quality assurance through the study. An overview of management and analysis of quantitative and qualitative data is also provided. Details of sample size determination, data collection tools and methods, data processing and analyses specific to the three research phases are discussed under the relevant chapters (chapters 4, 5 and 6 for the feasibility study (phase 1), design and internal validation

(phase 2) and implementation and evaluation (protocol manuscript drafted in **Annex 9**) (phase 3) respectively). The chapter concludes with a summary of the main points.

Chapter 4: Feasibility study This chapter reports on a feasibility study on the use of obstetric EWS in Nigeria. The chapter starts by providing a brief background on the rationale for the feasibility study, then presents the study objectives and describes the study design and data collection methods used. The chapter continues by describing the ethical considerations specific to this phase and measures taken to address potential limitations and ensure data quality. Data management and analysis are then described, and the chapter concludes by presenting and discussing the main findings of the feasibility study.

Chapter 5: Design and validation This chapter reports on the development and internal validation of a simple obstetric diagnostic prediction model and EWS for use in resource-limited settings (report submitted for publication, attached in **Annex 8**) (Umar A., Manu, A., et al*.,* 2019). The chapter provides the rationale for the analysis and describes the study design and data collection methods used. The process of design and validation of the EWS model, the resulting EWS model and proposed score-based monitoring chart for use in low-resourced settings described in detail. Next, the overall analysis and resulting EWS model are discussed in the context of the published evidence on EWS validation and effectiveness studies. The chapter ends with conclusions and a summary of key points.

Chapter 6: Implementation and evaluation Building on the developed and internally validated EWS chart presented in the previous chapter, this chapter describes the last phase of this PhD project. In this phase, the proposed score-based EWS monitoring chart was implemented and evaluated in a different cohort of obstetric patients using a longitudinal mixed-methods (quantitative and qualitative) study design. The chapter provides a description of the study design and objectives and the rationale for the data collection methods used. Additionally, it details sample size calculations, selection of participants, data collection, management and methods used for data analysis. Next, specific ethical considerations and steps

taken towards ensuring quality assurance are described. Finally, the findings are presented and the chapter ends with a summary of main points.

Chapter 7: Discussion This chapter discusses the results of the third phase of the PhD project (**Chapter 6**: Implementation and evaluation of EWS), in relation to key findings of the previous phases, and the wider literature on EWS in obstetrics (presented in **Chapter 2**). These are presented according to the specific objectives of the thesis. The chapter proceeds to discuss the strengths and limitations of the thesis as these affect interpretations of the main findings, then draws key conclusions, underscoring their applicability to other, similar settings. Finally, the unique contributions of the PhD to the body of knowledge is itemized, specific recommendations are made and the implications for future research is presented.

1.13. Role of the PhD candidate

The idea for this PhD research was conceived with my main PhD supervisor, Dr Charles Ameh, shortly after my induction as a PGR student in May 2017. Going forward, I developed the research concept, which was modified and structured into its current form with the help of the supervisory team (Dr Charles Ameh and Professor Matthews Mathai). Thence, I took the lead role in developing the research technical designs, Liverpool School of Tropical Medicine (LSTM) and in-country ethical clearance, field trips for data collection and analyses of the three study phases. Fieldwork was carried out by me and research assistants at different study sites in Nigeria. Additional travels were conducted to conferences and workshops within the UK. All other work (including data analyses and write-up of chapters) was carried out from my base at the Centre for Maternal and Newborn Health in LSTM. A summary of my contributions to each research activity and elements included in this thesis is provided as an annex (**Annex 1B**). Summary characteristics of the research team in terms of background, position, qualifications, research experience is provided as annex (**Annex 1C**).

1.14. Funding

This research was undertaken as a full-time PhD project at the Centre for Maternal and Newborn Health, Liverpool School of Tropical Medicine, University of Liverpool. The project was fully funded by the Nigerian Petroleum Trust Development Fund PhD scholarship scheme (ID 16PhD152). Additionally, some field trips for data collection were supported by the Centre for Maternal and Newborn Health, Liverpool School of Tropical Medicine, through the Johnson & Johnson's grant (charity number 222655) for improving the quality of care of maternal and newborn health (MNH) in Kwara state, Nigeria.

1.15. Chapter summary

Chapter 1: Introduction

- EWS are clinical tools that assign weighted values to physiological parameters based on degree of deviation from normal, and define a threshold beyond which mandatory actions must be taken to prevent irreversible morbidity or death.
- There are two types: single-parameter and aggregate-weighted EWS.
- In general, aggregate-weighted scoring systems have proved more sensitive than single-parameter EWS.
- EWS were first developed in 1997 by Morgan, Williams and Wright, and have been used in non-obstetric specialities since then.
- These EWS (developed by Morgan et al., 1997), however, failed to prove useful in obstetric patients, as the evaluation and triggering criteria that underlay their development did not account for the physiological changes related to pregnancy.
- Consequently, the UK Confidential Enquiry into Maternal and Child Health (CEMACH) in 2007 and 2011 recommended the use of early warning systems that are modified for obstetric populations.
- Several versions have been adopted in the UK and other well-resourced settings since the CEMACH recommendation: a 2014 survey revealed a 100% adoption rate in UK maternities, with the potential to improve clinical outcomes.
- There is evidence that transferring EWS generated in a developed country setting into a low-resource setting impacts negatively on its performance, hence the need for local validation before implementation.
- The development of EWS prediction models should involve statistical combination of predictor clinical observations into a multivariable model, which should then be validated.
- This research aimed to design and validate an obstetric EWS for use in low-resource settings with a view to improving quality of care and reducing the overwhelming burden of maternal morbidity and mortality in these settings.

Chapter 2: Systematic literature review

2.1. Overview of the chapter

This chapter presents the systematic literature review on use of EWS in obstetrics, conducted as part of this study. The aim of the systematic review was to update and synthesize the evidence on the usefulness of EWS in obstetric practice, and the feasibility of using EWS in low-resource settings. The chapter begins with the rationale for this review, then a method section describing how the review was conducted. In the results section, findings of the systematic review are presented in a narrative synthesis and complemented with tables, figures and charts. The discussion explains what the results mean: the major findings are discussed and situated in the context of wider literature on EWS. The strengths and limitations of the review are highlighted, and the chapter ends with a summary of key points from the review and a conclusion of the evidence.

2.2. Rationale for the review

Early warning systems are used in obstetrics to detect early clinical deterioration that triggers corrective clinical actions to avert morbidity and mortality. Several versions of obstetric early warning systems (early warning charts and an algorithm to trigger corrective action) are in use, but there is no international gold standard for use in obstetric practice. Obstetric EWS might be useful to improve the quality of care and reduce the risk of severe maternal morbidity and mortality, especially in resource-limited settings.

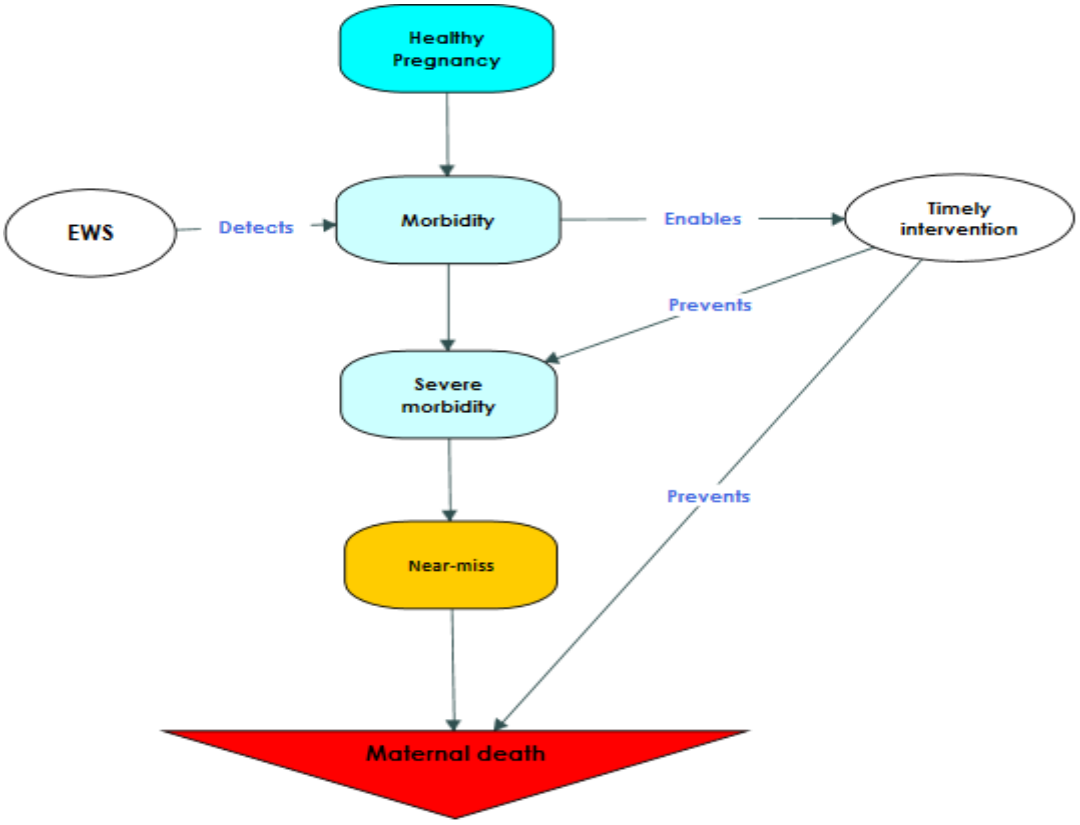
A systematic review of the effectiveness of obstetric EWS by Betesh and colleagues (2013) reported no direct evidence of improved clinical outcomes based on the two included observational studies with uncertain outcome measures (Betesh, Joel et al., 2013; Carle et al., 2013; Singh S et al., 2012). Since that review, however, several obstetric EWS studies have been conducted, assessing the diagnostic accuracy of obstetric EWC and the effectiveness of obstetric EWS in improving clinical outcomes. To the best of our knowledge, there has not been an up-to-date synthesis of evidence on the overall usefulness of obstetric EWS.

2.3. Hypothesis and review objectives

2.3.1. Hypothesis

The underlying hypothesis for this review was that an adverse pregnancy outcome is seen as a continuum of deteriorating events from healthy pregnancy to morbidity, severe morbidity, near miss and death if appropriate interventions are not instituted in a timely fashion (**Figure 2.1**). The "track and trigger" of physiological parameters on EWS can therefore aid in early recognition of morbidity, thus halting the cascade of severe maternal morbidity, near miss and mortality.

Figure 2 1 Hypothesis of the EWS intervention



2.3.2. Review objectives

The objectives of this systematic review were 1) to synthesize the evidence on effectiveness of obstetric EWC as screening tools for morbidity and mortality (predictive accuracy) and in improving clinical outcomes in obstetric populations; and 2) to determine the effectiveness of the EWS trigger systems and to explore the feasibility of implementing obstetric EWS in low-resource settings.

2.4. Methods

2.4.1. Registration

A study protocol was created for this systematic review (**Annex 2A**). In keeping with good and evidence-based practice, the review protocol was published in the International Prospective Register of Systematic Reviews (PROSPERO-CRD42017077504) (Umar A., Muriithi F. et al., 2017).

2.4.2. Study design

The design of this systematic review was based on the principles and methods provided by the York University's Centre for Reviews and Dissemination guideline (Khan et al., 2001). Narrative synthesis approach was employed to synthesize the selected studies in structured manner following the European Social Research Council guidance (Popay, 2006). The review findings were reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al, 2009).

2.4.3. Databases searched

A preliminary search was conducted for existing reviews in the Cochrane Central Register, the three databases of the Centre for Reviews and Dissemination (Database of Abstract of Reviews of Effectiveness, Health Technology Assessment Database, and the NHS Economic Evaluation Database), Turning Research Into Practice (TRIP) Database and for ongoing reviews in PROSPERO. Electronic search of Medline, CINAHL, Scopus, Science Direct and Science Citation Index was subsequently conducted for relevant primary research studies. These databases were selected based on their relevance to the topic as well as their wide geographical coverage.

We also searched reference lists of identified articles and professional society websites including World Health Organization (WHO), Royal College of Obstetricians and Gynaecologists (RCOG), American College of Obstetricians and Gynecologists (ACOG), Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) and South African Society of Obstetricians and Gynaecologists (SASOG) for relevant publications.

2.4.4. Criteria for study selection

All relevant studies published between January 1997 and March 2018 in any language were considered for inclusion. The year 1997 was selected as the starting point as EWS were first used in clinical practice in 1997 (Morgan & Williams, 1997). Study designs such as prospective and retrospective longitudinal, case-control, cohort, quasi-experimental, step-wedge and randomized controlled trials were considered relevant if they possessed the following characteristics:

Participants

Pregnant women in labour, sick pregnant women and women who had recently given birth (within 6 weeks after birth) admitted to hospital units including intensive care and high-dependency units.

Intervention

Obstetric early warning system, to include both paper-based and electronic monitoring systems.

Comparisons

Non-obstetric early warning systems, usual care practice.

Outcome measures

Clinical outcomes: Maternal death, non-severe maternal morbidity, potentially life-threatening conditions, maternal near miss, intensive care unit admission. Trigger system: referral to a specialist, referral for further care, the interval between a trigger and corrective clinical action.

2.4.5. Search strategy

We used search terms that comprised a combination of text words and synonyms related to the intervention and outcomes of interest (**Table 2.1**); these were reviewed by a systematic review expert at the Liverpool School of Tropical Medicine and pre-piloted before application on the relevant databases.

Table 2 1 Combination of search terms

Intervention terms	Outcome terms
"early warning"	"maternal mortality" (MeSH)
"early detection"	"maternal morbidity" (MeSH)
"track and trigger"	"obstet* complication"
"monitoring chart"	"obstet* haemorrhage"
"vital$ chart"	"matern* outcome"
EWS	"matern* sepsis"
MOEWS	"eclampsia"
MEOWS	"chorioamnionitis"

2.4.6. Study selection

Two reviewers independently screened all potentially relevant titles for eligibility. Publications were selected in two phases: first by review of titles and subsequently by full text review. List of papers to be included/excluded were compared. Differences in judgement were resolved through consensus, were feasible and/or in consultation with the PhD supervisory team. All studies that met the inclusion criteria were included. Authors of conference abstracts were contacted by email for full texts: where these are not available, abstracts were excluded.

Also, studies were excluded if they were a) Conducted on paediatric or non-obstetric adult population, b) Of qualitative methodological designs, c) Commentaries, editorials or letters.

Studies of qualitative methodological design were excluded as the review seeks to compare reported accuracy of EWS in predicting adverse obstetric outcomes in terms of screening characteristics (i.e sensitivity, specificity, positive and negative predictive values). We also aimed to potentially pool the effect estimates of EWS in improving measured outcomes using statistical meta-analysis where feasible (or descriptive statistics for heterogeneous outcomes). Finally, the robust quality assessment tool used to assess included studies for risk of bias and applicability concerns could not be applied to qualitative research studies. While this has significantly eased our analysis and reporting of the synthesised evidence, we

acknowledge the potential drawbacks of excluding the qualitative studies, including missing evidence on potential factors that could affect implementation of the tool.

2.4.7. Data extraction

Study title, authors, design, setting, population, description of intervention used, outcomes and summary of findings of included studies were abstracted onto a pre-agreed Microsoft Excel data abstraction sheet that was thoroughly cross-checked and ratified by two reviewers (**Annex 2B**: Summary table for screening of studies).

2.4.8. Quality assessment

Based on one of the objectives of this systematic review - to synthesize evidence on the diagnostic accuracy of obstetric EWS - the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool was used for assessing quality of included studies. QUADAS-2 defines quality in diagnostic accuracy studies as the degree to which the estimate of diagnostic accuracy avoids the risk of bias, and the extent to which included studies are applicable to the review's research questions. The QUADAS-2 tool comprises four domains: patient selection, index test, reference standard, and flow of participants. Each domain is assessed in terms of risk of bias, and the first three domains are also assessed in terms of concerns regarding applicability to the systematic review's objectives. Signalling questions are suggested by the QUADAS-2 authors to help ensure a most transparent rating of bias and applicability of primary diagnostic accuracy studies. The tool is applied in four phases: summarizing the review questions, tailoring the tool to produce review-specific signalling questions and scoring guidance, constructing a flow diagram for the primary studies, and judging bias and applicability based on the scoring guidance. The included studies were assessed for risk of bias across the four domains and flow of participants across the three relevant domains. In accordance with the QUADAS-2 guidelines, the suggested signalling questions (**Table 2.2**) were tailored to fit our review.

2.4.9. Data analysis

A structured narrative synthesis of included studies was conducted using the European Social Research Council guidance on the conduct of narrative synthesis in systematic reviews (Popay et al., 2006). Included studies were tabulated by study objective and or study population to produce a clear descriptive summary. Relationships were explored within and between included studies, themes and

subthemes were identified and organized to fit into the review's objectives. The evidence was synthesized to provide a meaningful narrative and results were presented and discussed.

Table 2 2 Quality assessment tool

Domain	Signalling questions	Scoring
Patient selection	Was a continuous or random sample of	Yes
Risk of bias	participants enrolled?	No
		Unclear
	Did the study avoid unnecessary exclusions?	Yes
		No
		Unclear
Applicability	Are there concerns that the included	Yes
concern	participants do not match the review	No
	questions?	Unclear
Index test	Were the reference range adjusted for	Yes
Risk of bias	physiological change in pregnancy?	No
		Unclear
	Was the trigger threshold pre-specified?	Yes
		No
		Unclear
Applicability	Are there concerns that the index test, its	Yes
concern	conduct or interpretation differ from review	No
	questions?	Unclear
Reference	Is the index test compared to a reference	Yes
standard	standard	No
Risk of bias		Unclear
	Were the reference standard results	Yes
	interpreted without knowledge of the results	No
	of the index test	Unclear
Applicability	Are there concerns that the target condition	Yes
concern	as defined by the reference standard does not	No
	match the review questions?	Unclear
Flow of	Is the attrition rate acceptable (<20%)?	Yes
participants		No
Risk of bias		Unclear
Applicability	Could the drop-out participants or missing	Yes
concern	data be systematically similar to those who	No
	completed?	Unclear

The signalling questions in our contextualized QUADAS quality assessment checklist (**Table 2.2**) were incorporated into a pre-agreed Excel data-extraction sheet. Included studies were subsequently assessed for quality across the relevant domains as having a high, low or unclear risk of bias/concerns about applicability based on our adopted scoring guideline (**Table 2.3**).

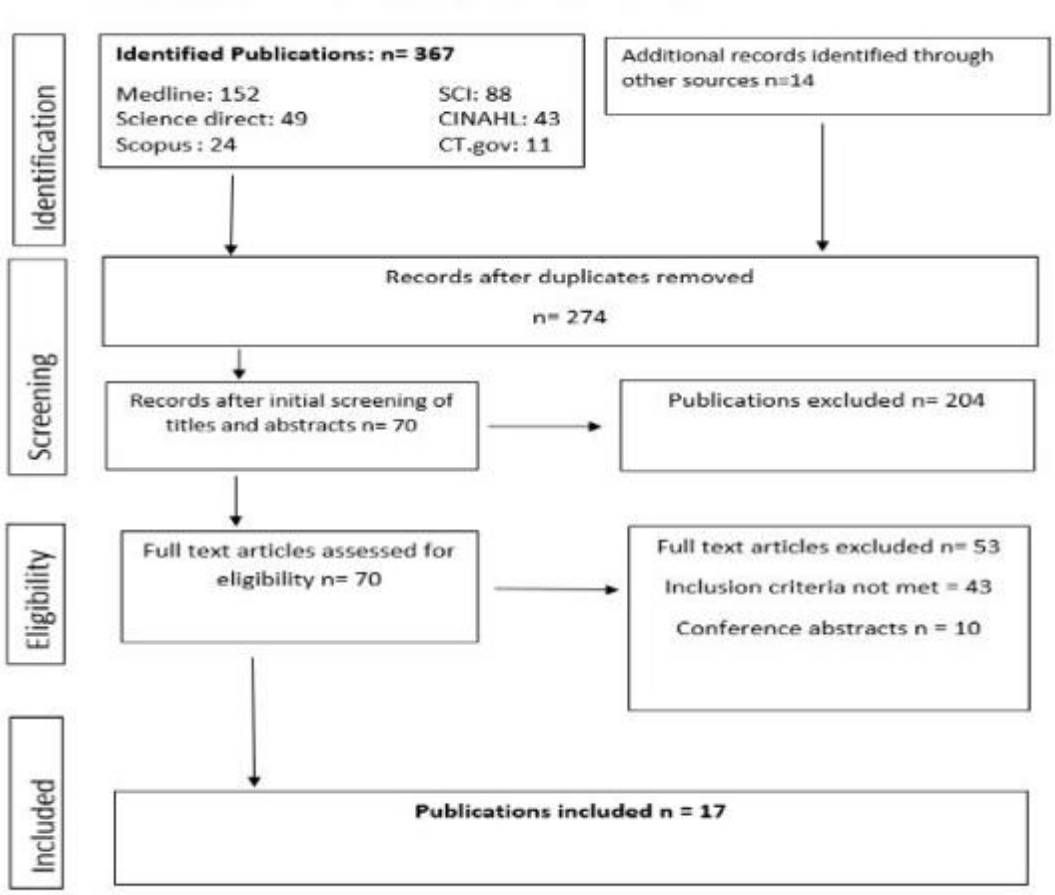
Table 2 3 QUADAS-2 Scoring guideline (order of answers not important)

	Risk of bias	
Score	**Question 1**	**Question 2**
Low	Yes	Yes
	Yes	Unclear
High	No	No
	No	Unclear
Unclear	Yes	No
	Unclear	Unclear
	Concern about applicability	
Score	**Answer**	
Low	Yes	
High	No	
Unclear	Unclear	

2.5. Findings

Our search identified 381 papers (Medline = 152, Scopus = 24, CINAHL = 43, Science Citation Index = 88, Science Direct = 49, Clinicaltrials.gov = 11 and other sources = 14). A total of 107 duplicates were removed. Ten publications were available only as conference abstracts; authors of six of these abstracts confirmed unavailability of full texts. Seventeen papers met the inclusion criteria and were included in the review (**Figure 2.2**).

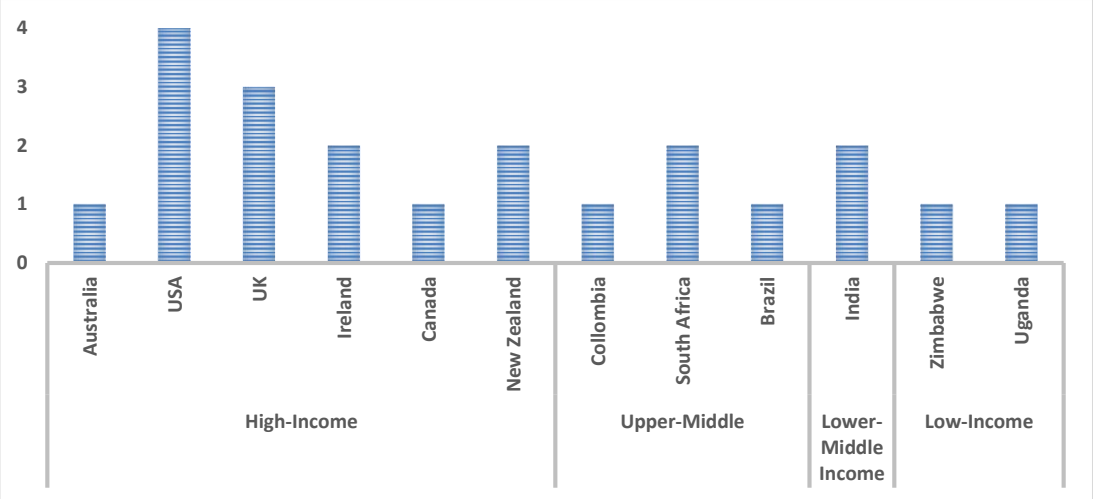
Figure 2 2 PRISMA diagram for article selection process



2.5.1. Characteristics of included studies

The 17 studies included in the review were conducted in six high-income countries, three upper-middle-income counries, one lower-middle-income and two low-income countries according to World Bank classification (**Figure 2.3**) (World Bank, 2018). Two studies included multiple countries. One of these (Von Dadelszen et al., 2011) was located in four high-income countries (Canada, Australia, New Zealand and the UK), while the second study (Payne et al*.,* 2014) recruited participants from six low- or middle-income countries, including India, Pakistan, Zimbabwe, Columbia, South Africa and Brazil.

Figure 2 3 Distribution of included studies by country and income status



Included studies fell into two thematic categories: 1) studies that tested predictive accuracy of EWS on adverse obstetric outcomes (validation studies) and 2) studies testing effectiveness of EWS on measured outcomes. The study characteristics, including design, participants, intervention, outcome measures and key findings of these studies are presented in **Table 2.4**, according to the two themes. All reviewed studies were published between 2010 and 2017. Although no language barrier was applied to our search, included studies were all available in English language.

Table 2 4 Summary of included studies within the two review themes

Theme 1	Studies that tested predictive accuracy of EWS on adverse obstetric outcomes				
Publication	**Design**	**Participants**	**EWS type**	**Outcomes**	**Findings**
Lappen RJ et al., 2010	Retrospective cohort	Women with chorioamnionitis (n=913)	MOEWS and SIRS	Severe sepsis, ICU transfer, death	Both performed poorly (MOEWS PPV <5.4%, SIRS Specificity=17.6%)
Von Dadelszen P et al., 2011	Prospective Multicentre cohort study	Women admitted with pre-eclampsia or who developed pre-eclampsia in hospital (n= 1935)	fullPIERS model	Death, 1 or more serious CNS, cardiorespiratory, hepatic, renal, or haematological morbidity	Predicted adverse maternal outcomes with AUROC of 0.88 (95% CI 0.84-0.92)
Singh S et al., 2012	Prospective observational study	Obstetric admissions from 20 weeks through to puerperium	CEMACH MEOWS	Morbidity based on consensus	Sensitivity 89%, Specificity 79% PPV 39%, NPV 98%
Carle C et al., 2013	Retrospective analysis of secondary data	Obstetric admissions (n=4440) to ICU	ICNARC obstetric EWS	Maternal death	AUROC Statistical EWS = 0.995 Clinical EWS = 0.957
Payne BA et al., 2014	Prospective Multicentre cohort study	Women (n = 2081) with any hypertensive disorder of pregnancy admitted to a participating centre	miniPIERS model	Death, 1 or more serious CNS, cardiorespiratory, hepatic, renal, or haematological morbidity	Predicted adverse maternal outcomes with AUROC of 0.77 (95% CI 0.74-0.80)
Edwards ES et al., 2015	Retrospective cohort	Women with chorioamnionitis (n=913)	Six published MOEWS charts	Severe sepsis, death	AUROCs are: A=0.65 B = 0.52 C = 0.52 D = 0.72 E = 0.68 NEWS = 0.95 F = 0.65
Singh A et al., 2016	Prospective observational study	women in labour beyond 28 weeks gestation, up to 6 weeks post-partum (n=1065)	CEMACH MEOWS	Morbidity based on consensus	Sensitivity 86.4% Specificity 85.2% PPV 53.9% NPV 96.9%

Hedriana HL et al., 2016	Retrospective case–control study	Cases; Obstetric admissions to ICU (n=50), Controls; SVD (n=50)	MEWT	ICU admission	Sensitivity 72% Specificity 96% PPV 95% NPV 77%
Shields E L et al. 2016	Quasi-experimental	Obstetric admissions in six hospitals n=11399	MEWT	ICU admission	Sensitivity 97% Specificity 99% PPV 12% NPV 99%
Ryan HM et al., 2017	Retrospective case–control study	Cases; 46 obstetric admissions to ICU, Controls;138 admissions no critical care	CEMACH MEOWS	ICU admission for longer than 24 hours	Sensitivity 96% Specificity 54% PPV 41% NPV 97%
Paternino-Caicedo et al., 2017	Retrospective cohort study	Pregnant and post-partum women (up to 42 days) admitted into the ICU (n=702)	ICNARC obstetric EWS	Maternal death	AUROC 0.84
Nathan HL et al., 2017	Prospective cohort	Women with pre-eclampsia at admission (n=1547)	CRADLE Vital Signs alert EWS	Kidney injury, MgSO4 use and ICU admission, maternal death	Trigger predicted increased risk of Kidney injury (OR 1.74), MgSO4 use (OR 3.4) and ICU admission (OR 1.5)
Theme 2	Studies testing effectiveness of EWS in improving measured outcomes in obstetric population				
Publication	**Design**	**Participants**	**EWS**	**Outcomes**	**Findings**
Austin DM et al., 2013	Mixed retrospective (before) and prospective (after) design	Retrospective (n=42) and prospective (n=71) obstetric admissions	EWS	Severity of morbidity	MDT review determined that EWS might have reduced severity of morbidity, no formal stats test
Maguire PJ et al., 2015	Mixed retrospective (before) and prospective (after) design	Obstetric patients with bacteraemia before (n=61) and after (n=20) IMEWS	IMEWS	Vital signs recording and trigger/antibiotic time lag	Improvement in RR recording ($p<0.05$) and reduction in time between trigger and antibiotics ($p>0.05$)
Maguire PJ, 2016	Retrospective observational study	Women monitored with IMEWS (n=80) and other	IMEWS	ICU Admission	IMEWS contributed to early recognition of

		methods (n=87) before ICU admission			critical illness but cannot replace clinical judgement
Shields E L et al., 2016	Quasi-experimental	Obstetric admissions in six hospitals n=11399	MEWT	Morbidity, ICU admission	Reduction in morbidity (p=0.01) and ICU admission (p=0.8)
Sheikh S et al., 2017	Before–after Quasi-experimental	Women who had CS before (n=100) and after (n=100) implementation of NEWS	NEWS	Need for specialist review, ICU admission, referral due to post-op complications	All reduced but no statistical tests
Merriel A et al., 2017	Before–after Quasi-experimental	Women undergoing CS before (n=79) and after (n=85) implementation	MEOWS	Preoperative stabilization, action taken due to trigger	Significant improvement in the two outcomes (p<0.05)

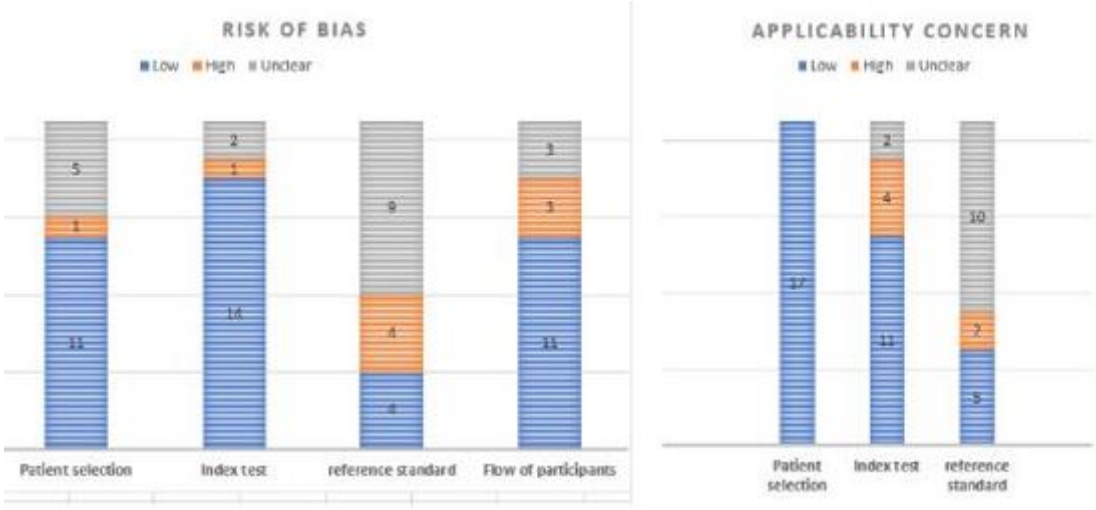
Eleven studies (Payne et al, 2014; Carle et al., 2013; Edwards et al., 2015; Hedriana et al, 2016; Lappen et al, 2010; Nathan et al, 2017; Paternina-Caicedo et al., 2017; Ryan et al., 2017; Singh A et al, 2016; Singh S et al., 2012; Von Dadelszen et al., 2011) assessed clinical utility of early warning systems as screening tools for obstetric morbidity (predictive accuracy); 6 of these (Singh et al., 2012; Carle et al., 2013; Singh et al., 2016a; Hedriana et al., 2016; Paternina-Caicedo et al., 2017; Ryan et al., 2017) investigated accuracy of the tools in predicting outcomes among all obstetric inpatients. The remaining five studies were conducted in patients with specific forms of obstetric complications; Two of these studies (Edwards et al., 2015a; Lappen et al., 2010) focused on women with chorioamnionitis, while women diagnosed with pre-eclampsia constitute the study population in the remaining three validation studies (Payne et al, 2014; Nathan et al., 2017; Von Dadelszen et al., 2011).

Five studies (Austin et al., 2014; Maguire et al., 2015; Maguire et al., 2015; Merriel et al., 2017; Sheikh et al., 2017) tested effectiveness of EWS in reducing prevalence of measured outcomes. One study (Shields et al, 2016) assessed both clinical utility of EWS in screening and their effectiveness in improving outcomes in obstetric population.

2.5.2. Quality of included studies

Based on the QUADAS-2 tool, a summary of quality of all included studies is presented in **Figure 2.4**, while detailed assessment of the quality of each included study (risk of bias and concern about applicability) is provided as an annex (**Annex 2C**: Quality of individual studies).

Figure 2 4 Quality assessment of included studies (n=17)



Risk of bias

Majority of the studies had low risk of bias for patient selection (n=11, 64.7%), index test (n=14, 82.4%) and flow of participants (n=11, 64.7%). The most common source of high risk of bias was absence of reference standard (4 studies, 23.5%), followed closely by flow of participants or attrition bias in three studies (17.6%). Just over half of the included studies (9, 52%) had unclear rik of bias for reference standard. This was commonest among studies that assessed effectiveness of early warning systems on measured outcomes (**Appendix 2C**: Quality of individual studies).

Concern about applicability

All studies included participants who were applicable to our review's questions (100% low concern about applicability for patient selection). There was high concern about applicability of EWS charts used in four studies (Lappen et al., 2010; Von Dadelszen et al., 2011; Payne et al., 2014; Nathan et al., 2017). One study (Lappen et al., 2010) used a chart whose parameters were not modified for use in obstetric population. Nathan and colleagues (Nathan et al., 2017) used a single-parameter (blood pressure only) early warning tool to predict adverse outcomes in patients with pre-eclampsia.

The studies on Pre-eclampsia Integrated Estimate of Risk (fullPIERS and miniPIERS) models generated a good quality evidence from two multi-country prospective cohort studies (Payne et al, 2014; Von Dadelszen et al., 2011). The two statistically derived early warning models generated in these studies were designed for use in

pre-eclampsia patients, who constituted the derivation population. The models included laboratory investigations, and other clinical signs in addition to patient vital signs. These parameters may not be applicable to all obstetric patients, particularly those with conditions other than hypertensive diseases of pregnancy, hence the concern about applicability to this review.

2.5.3. Diagnostic accuracy of EWS

Seven of the 11 included studies that tested the effectiveness of EWS in predicting obstetric morbidity/mortality had death as a primary outcome (**Table 2.4**).

Accuracy in predicting maternal death

Two studies (Carle et al., 2013; Paternina-Caicedo et al., 2017) were retrospective, of good or moderate quality (**Annex 2C**: Quality of individual studies) and were on general obstetric population. Carle and colleagues (Carle et al., 2013) modelled EWS parameters to predict maternal death using secondary data on women admitted to intensive care from the UK Intensive Care National Audit and Research Centre data set. The model had high predictive accuracy for death with an area under the ROC curve of 0.96 (95% CI 0.92–0.99). Similarly, the early warning chart recommended by the 2005 CEMACH report was 94% accurate in predicting maternal death (AUROC 0.94, 95%CI, 0.88–0.99) using this data set. The second study (Paternina-Caicedo et al., 2017) performed an external validation of the chart produced by Carle and colleagues on 702 pregnant and post-partum women admitted to intensive care in a tertiary hospital in Colombia; they reported a reduced, but equally good predictive accuracy (AUROC = 0.84, 95%CI, copy) for maternal death, need for mechanical ventilation or vasoactive support.

Five studies were on specific obstetric populations, these studies had a high risk of bias or concern for applicability (Lappen et al., 2010; Von Dadelszen et al., 2011; Payne et al., 2014; Edwards et al., 2015a; Nathan et al., 2017) (**Annex 2C**: Quality of individual studies). Three of these were large prospective studies that focused on women with pre-eclampsia and reported high sensitivity (>85%), specificity (>75%) and discriminatory ability (AUROC >0.75) of EWC in predicting death (Beth A. Payne, 2014; Nathan et al., 2017; Von Dadelszen et al., 2011). Two retrospective studies with only women with pregnancy-related sepsis, showed that EWS did not

accurately predict death (PPV <1%, AUROC < 0.75) (Edwards et al., 2015a; Lappen et al., 2010).

Accuracy in predicting morbidity and ICU admission

Five studies (Hedriana et al., 2016; Ryan et al., 2017; Shields et al, 2016; Singh A et al., 2016; Singh S et al., 2012) reported the accuracy of obstetric EWS in predicting increasing severity of obstetric morbidity or ICU admission. General obstetric study populations were used in three of these studies (Hedriana et al., 2016; Ryan et al., 2017; Shields S et al, 2016). Although these studies were of varying quality, they reported that EWC had a very high median (interquartile range) sensitivity of 89% (72% to 97%) and specificity of 85% (67% to 98%). The median (interquartile range) positive predictive values were low - 41% (25% to 74%) (**Table 2.4**).

Two retrospective cohort studies reported very poor predictive accuracy (positive predictive values less than 1% and AUROC of less than 0.75) of obstetric EWC for severe sepsis among cohorts of women with chorioamnionitis (Lappen et al., 2010; Nathan et al., 2017) (**Table 2.4**). The sensitivities ranged from 40 to 100%, and specificities varied even more ranging from 4 to 97%. However, the data set used in the two studies had a high risk of attrition bias as more than 50% of the participants had incomplete vital signs records and were excluded from the analysis (**Annex 2C**: Quality of individual studies).

The two multi-country prospective cohort studies on pre-eclampsia risk prediction models (fullPIERS and miniPIERS) with robust sample sizes reported accuracy of 88% and 77% in predicting adverse outcomes among women with pre-eclampsia in well-resourced (Von Dadelszen et al., 2011) and low-resourced (Payne et al., 2014) settings respectively.

2.5.4. The effectiveness of EWS on measured outcomes

Six studies (**Table 2.4**) assessed effectiveness of EWS in improving outcomes in obstetric population. We initially planned to carry out a meta-analysis, but because the outcomes were heterogeneous (**Table 2.5**) and report of effect estimates were limited, this was not feasible. A careful narrative analysis was therefore performed, and findings are reported based on these outcomes. The outcome measures included clinical outcomes (obstetric morbidity, maternal death, and ICU

admission) and trigger system measures (vital signs recording, the time lag between the trigger and corrective clinical action, preoperative stabilization, need for specialist review and referral rate) (**Table 2.5**).

Table 2 5 Outcomes assessed by the EWS effectiveness studies (n=6)

Publication	Outcome measures						
	Morbidity	ICU admission	Maternal death	Vitals recording	Time lag	Preop stabilization	Referral rate
Shields, E. L., et al., 2016	✓	✓					
Maguire, P. J., et al., 2015				✓	✓		
Maguire P. J., et al., 2015		✓					
Sheikh, S., et al., 2017		✓	✓				✓
Merriel, A., et al., 2017						✓	
Austin, D. M., et al., 2013	✓						

Maternal morbidity, death and ICU admission

Only one before and after quasi-experimental study in patients who had had caesarean section had maternal death as an outcome measure (Sheikh et al., 2017). In that study, two periods compared were not equal, it was unclear if the sample was large enough to detect any difference in the outcome. However, there was a significant reduction in complications due to PPH after EWS introduction (**Table 2.4**). The reduction in PPH after the introduction of the EWS compared to before was attributed to early recognition and timely management.

In a large quasi-experimental trial (Shields et al, 2016), there was significant reduction in CDC-defined severe and composite maternal morbidity ($p<0.01$), but not mortality in six intervention hospitals following EWS implementation, compared to 19 control hospitals where the two outcomes remained unchanged. However, ICU admission rate was unaffected in both trial arms. Also, there was no change in the ICU admission rate in the intervention and control hospitals (Shields et al, 2016).

Reduction in ICU admission and severity of obstetric morbidity were also reported after implementation of EWS in two before and after quasi-experimental studies (Austin et al., 2014; Maguire et al., 2015). However, the reported effect estimates in both studies could not reach statistical significance (p>0.05) (**Table 2.4**).

EWS triggered actions;

One single centre before and after study (Maguire et al*.,* 2015) reported increase in the documentation frequency of patient vital signs following implementation of the Irish Maternity Early Warning System. This was especially so for respiratory rate. The authors also reported a statistically significant reduction in the time interval between EWS trigger and antibiotic administration among obstetric patients with bacteraemia. It must, however, be noted that the sample size was small, especially in the post-implementation (n=20) group.

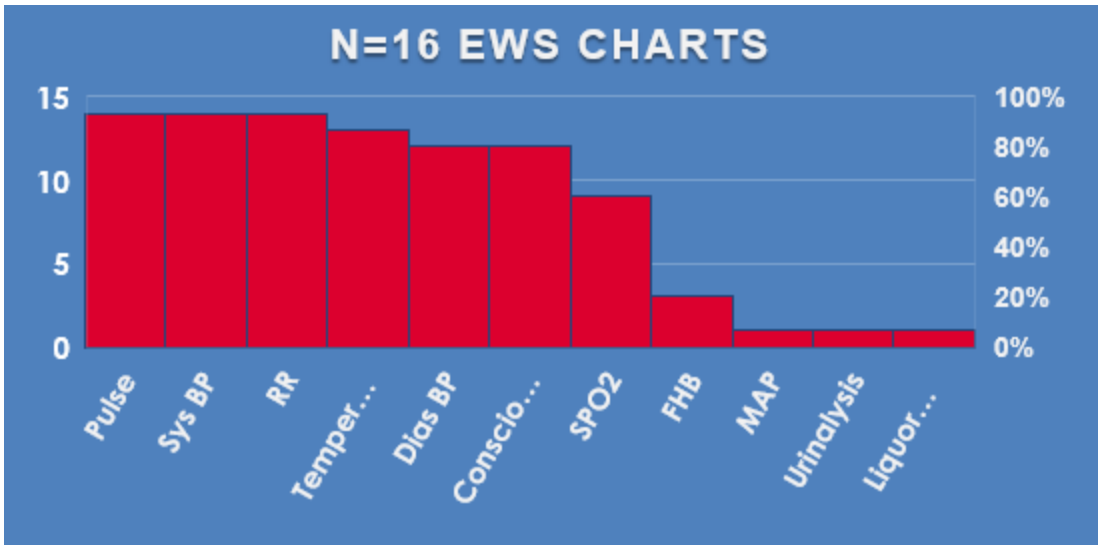
Preoperative stabilization of women undergoing caesarean was reported to have significantly improved after implementation of EWS (odds ratio 2.78, 95%CI, 1.39-5.54) (Merriel et al., 2017). Also, there were improvements in care triggered by abnormal early warning chart observations in 68% of patients after EWS implementation compared to only 4% before implementation of the tool (p<0.001).

In another before and after quasi-experimental study (before n=100, after n=100), Sheikh and colleagues reported a non-statistically significant reduction in the need for specialist review (Sheikh et al., 2017). Similarly, there was non-significant higher-level referral rate due to post-operative complications among women who had a caesarean section, after implementation of EWS.

2.5.5. EWS parameters

Details of 16 versions of EWS were obtained from the reviewed studies. The components of a hospital-specific EWS used in one study (Merriel et al., 2017) were not reported and could not be deciphered from the paper. There were variations in parameters included among the reviewed charts (**Figure 2.5**); however, 14 of these charts had pulse rate, systolic blood pressure, and respiratory rate, 13 charts had temperature and 12 charts had diastolic blood pressure and consciousness level. On average four in five charts identified in this review (mean, 82.5%; n=16) had these five parameters.

Figure 2 5 Early warning parameters



2.6. EWS parameters and sepsis

Maternal sepsis is a leading direct cause of preventable maternal morbidity and mortality. The physiological changes of pregnancy can mimic the early stages of sepsis and can also accelerate its progress (Lukas et al, 2012). These factors can delay the recognition of sepsis until severe deterioration has occurred. The early detection of sepsis is therefore key to optimizing outcomes.

In the non- obstetric population, the modified early warning score (MEWS) has been shown to predict intensive care unit (ICU) transfer and mortality (Subbe et al, 2001; Kobblinsky et al, 2012). However, when the same system was applied to an obstetric population with infection, the predictive power was found to be poor (Lappen et al, 2010).

Similarly, systemic inflammatory response syndrome (SIRS) is a specialised form of EWS for sepsis, that incorporates temperature, heart rate, respiratory rate and white blood cell count (Cantwel et al, 2011). At least two of the 4 SIRS criteria must be abnormal to define sepsis. In a large retrospective observational study involving 913 obstetric admissions with chorioamnionitis, SIRS criteria performed poorly (PPV= 0.9%) in predicting risk of ICU admission, sepsis or death (Lappen et al, 2010).

Another retrospective cohort study that used prospectively collected clinical observations at a single tertiary unit in America compared the predictive power of published modified obstetric EWS for the development of severe sepsis in women

with chorioamnionitis (Edwards et al, 2015). Six different EWS versions were identified which varied widely in terms of alert thresholds, format, and accuracy. All these charts performed poorly in predicting severe sepsis in this group of obstetric patients; in general, severe sepsis was over detected (Edwards et al, 20115).

Overall, there is limited evidence on effectiveness of EWS parameters in obstetric population with sepsis. While Lappen and colleagues (2010) suggested that SIRS and MEWS should not be used in cohorts of obstetric patients with sepsis, Edwards et al (2015) opined that Simple EWS with high sensitivity, followed with more specific secondary testing is likely to be the best way forward in such settings.

2.7. Effectiveness of Partograph on outcomes

Like obstetric EWS, the partograph appears to work as a trigger for referral and transfer, which is one of its primary purposes (Opiah et al, 2012). Although WHO has recommended its universal use, a Cochrane review in 2013 has concluded that overall use of the partogram did not significantly impact on several perinatal and maternal outcomes (Lavender et al, 2013). This conclusion was based on six randomized trials from both high and low resource settings.

For pregnant women without risk factors at the onset of spontaneous labour, partograph defined cervical dilatation patterns that should result in normal birth outcomes. Evidence on the diagnostic test accuracy of using the 1-cm/hour threshold to diagnose risk of adverse birth outcomes was derived from a systematic review that included eleven observational studies, involving over 17,000 women, which were conducted in Brazil, Ecuador, India, Indonesia, Iran, Malaysia, Mali, Nigeria, Senegal, South Africa, Thailand and Uganda (Wei S et al, 2013).

Outcome measure used in these studies was adverse birth outcome which was defined using different criteria. These included Apgar score less than 7 at 1 minute, Apgar score less than 7 at 5 minutes, birth asphyxia, and composite adverse outcomes including fresh stillbirths and neonatal resuscitation, fresh stillbirths and Apgar score of 7 or less at 1 minute, fresh stillbirths and Apgar score less than 7 at 5 minutes, fresh stillbirths and birth asphyxia, and severe adverse birth outcome

(the latter defined as occurrence of any of the following: stillbirth, early neonatal death, neonatal use of anticonvulsant, neonatal cardiopulmonary resuscitation, Apgar score less than 6 at 5 minutes, maternal death or organ dysfunction associated with labour dystocia, or uterine rupture) (Wei S et al, 2013).

The findings from this review suggest that the sensitivity of the 1-cm/hour threshold ranges from 28.8% to 100.0% and the specificity ranges from 22.8% to 93.1%, depending on the reference standard applied. Findings from the largest study (n = 8489 women) with an adverse birth outcome rate of 2.3%, and a sensitivity and specificity of 56.7% (95% CI 49.7–63.5%) and 51.1% (95% CI 50.1–52.2%), respectively, show that using the 1-cm/hour dilatation rate threshold may correctly identify 6 out of 10 women with adverse birth outcomes (true positive) when the population prevalence of adverse birth outcomes is 1% (10 per 1000 births), or 28 out of 50 women with adverse birth outcomes when the population prevalence of adverse birth outcomes is 5% (50 per 1000 women) (low-certainty evidence). This test strategy may miss 4 out of 10 women with ABOs (false negative) when the population prevalence of ABOs is 1%, or 22 out of 50 women when the population prevalence of adverse birth outcomes is 5% (low-certainty evidence). In addition, the test strategy may incorrectly identify 484 out of 990 women without adverse birth outcomes as being at risk when they are not (false positive) when the population prevalence of adverse birth outcomes is 1%, or may incorrectly identify 465 out of 950 women without adverse birth outcomes as being at risk when they are not when the population prevalence of ABOs is 5% (low-certainty evidence). As a consequence of such misclassification, a large proportion of women without a true risk of adverse birth outcomes could be offered inappropriate, unnecessary and potentially harmful labour interventions (Wei S et al, 2013). Having mentioned the above however, in 2018 Cochrane review, the authors concluded on the basis of their findings that they cannot be certain on the effects of routine use of the partograph as part of standard labour management and care, or which design, if any, are most effective. Further trial evidence is required to establish the efficacy of partograph use per se and its optimum design (Lavender et al, 2018).

2.8. Uptake of partograph in LMICs and challenges

Over 25 years ago, the World Health Organization declared the partograph to be an essential tool for monitoring and management of labour, hence, exclusively for use in labouring women (Mathibe-Neke 2009). Correct use of the partograph has been shown to be beneficial in differentiating abnormal labour progress, and prevention of complications due to obstructed and prolonged labour (Mathai M 2009; Masika M 2015). There is also evidence from observational studies to suggest that midwives find the partograph to have practical benefits in terms of ease of use, time resourcefulness, continuity of care and educational assistance (Lavender et al, 2013).

Despite established evidence of safe and successful labour with the use of the partograph, this tool remains inconsistently and incorrectly applied and used (Ogwang, 2009; Wakgari et al, 2015). Usage rage is generally low, especially in low resource settings; two large cross-sectional studies reported 40.2% usage rate in Ethiopia, and 5-33% among tertiary hospitals in Nigeria (Fawole et al, 2008; Lavender et, al 2013). Similarly, a study conducted in Uganda found that in two large referral health facilities only 23.9% and 18.3% of births were monitored using a partograph (Wakgari et al, 2015).

Use of the Partograph for monitoring active labour has been described as generally problematic: studies conducted in Nigeria concluded that the lack of knowledge about and training in the use of this tool limited the correct use and often resulted in non-use among health workers (Yang et al, 2017; Fawole et al, 2008; Oladapo, 2006). Other reported barriers to effective utilization of the partograph include non-availability of the charts in the labor wards, (Oladapo et al, 2006; Umezulike 1999), lack of adequate number of health care personnel, and perception that it is time consuming to use in the light of staff shortage (Nakkazi S, et al 2001), lack of understanding of the relevance of the partograpgh in preventing obstructed labor (Oladapo 2006). Other factors include lack of standard institutional guidelines on the use of the partograph in labor, lack of support from management in terms of providing essential supplies, leading to lack of motivation of the health workers (Kawuwa, et al 2006).

A 2014 systematic review by Ollerhead and colleagues reported that most of the barriers to effective utilization of partograph affected local practice in LMICs (Ollerhead E et al, 2014). These factors, according to the authors, related to the professional and practice environment of obstetric care, rather than to the evidence base. Partographs needed to be available, with appropriate equipment and clinical supplies for assessing progress in labour, and the resources to provide recommended interventions. Professionals might lack awareness, knowledge and training, and under-value partographs, seeing completion as complex and time-consuming rather than assisting good practice. Hence, they suggested that a supportive professional environment from peers and leaders, with quality assurance systems is necessary to promote partograph use in LMIC settings (Ollerhead E et al, 2014). Other measures including, adaptation to the local context in terms of both language and clinical practice, empowerment of women to expect better care, with delivery at health facilities and earlier admission, are also suggested by the review authors to as potential means to increase future partograph use (Ollerhead E et al, 2014).

2.9. Discussion

This systematic review did not identify any randomized controlled trials on EWS. It included 17 studies, mostly observational studies (Moher et al., 2009) and only two of all included studies were conducted in low-income countries. All studies that assessed the predictive accuracy of EWS for adverse obstetric outcomes were observational studies. Most of the studies that assessed the effectiveness of EWS in improving clinical outcomes were of quasi-experimental design.

For a screening tool to be of value, it should be safe to use, cost effective, accurate and acceptable to care, providers. The accuracy of an early warning chart to predict morbidity is indicated by the positive predictive value (PPV) or negative predictive value (NPV). Both of these are dependent on the prevalence of the condition. While it is desirable that a screening test should have a high sensitivity and specificity, the probability of a positive result when the condition actually exists (PPV) or the probability of a negative result when the condition does not exist (NPV) is equally

important. A screening tool for a condition of low prevalence, with high sensitivity and specificity, will likely have a low PPV and a high NPV. While for more common conditions, a screening test/tool with similar sensitivity and specificity will likely have a high PPV and a low NPV.

Early warning systems developed using a statistically derived model for obstetric population admitted to the critical care unit are accurate in predicting death (AUROC >0.80) (Paternina-Caicedo et al., 2017). In other general obstetric population, EWS was shown to be highly sensitive and specific in predicting morbidity and ICU admission, with comparatively low PPV (average of 41%). With a low probability that subjects with a positive screening test are truly at risk of deterioration (low PPV), there is the risk of unnecessary use of resources when protocols are triggered due to a "positive" test. Similarly, EWS with low NPV may miss many women who are likely to deteriorate clinically by giving them a false reassurance, and potentially resulting in catastrophic outcomes.

One low-quality multicentre controlled trial reported that obstetric EWS significantly reduces CDC-defined maternal morbidity but not ICU admission rate (Shields et al., 2016). A reduction in ICU admission will have been expected because the implementation of corrective measures may reduce the need for ICU admission however the management of women who are predicted to develop morbidity may be best in the ICU. Also, ICU admission rate may not be a good outcome measure because the criteria for ICU admission may vary.

The low positive predictive values for severe morbidity and ICU admission (PPV 41%) means that approximately, only one in two cases with a positive screening test is truly at risk of deterioration. As pointed out by Friedman (2015b) a warning system with a high false positive rate, may potentially worsen clinical care, constitute a nuisance alarm and contribute to alarm fatigue.

However, the relatively low positive predictive value for obstetric morbidity and ICU admissions reported in this review is comparable to other non-obstetric aggregated and single-parameter early warning systems (Alam et al., 2014; Smith et al, 2013b). Hence, as with these non-obstetric EWS, and as pointed out by Maguire and

colleagues (Maguire et al., 2016) obstetric EWS needs to be used with, and do not substitute, clinical judgement in patient monitoring and care.

Based on one small sample low-quality quasi-experimental study, there is no evidence that EWS reduces maternal deaths (Sheikh et al., 2017).
There is some evidence from small sample size, low-quality studies that introduction of EWS improves the quality of care for obstetric patients. Specifically, EWS significantly improves the frequency of vital signs observation, and improves pre-caesarean section stabilization of patients (Merriel et al., 2017; Sheikh et al., 2017). Also Maguire et al. in a small sample before–after study, reported that EWS reduces the time interval between abnormal vital signs and implementation of corrective clinical action but this was not statistically significant (Maguire et al., 2015).

There are some conflicting findings, particularly on the use of EWS in women with chorioamnionitis. Lappen et al (Lappen et al., 2010) and Edwards and colleagues (Edwards et al., 2015b) reported very poor performance for predicting sepsis in women with chorioamnionitis and argued that the EWS should not be used in this population. However, the findings were not surprising because information of vital signs was missing from records of 549 of the 913 women and was excluded from the analysis (Edwards et al., 2015; Maguire et al., 2015). For this reason, we assessed the two studies as having a high risk of attrition bias; **Table 2.2**).

Fourteen of the 16 EWS versions identified in this review included five parameters; the pulse rate, respiratory rate, temperature, blood pressure, and consciousness level. These parameters need simple patient monitoring devices that are readily accessible (BP machine, a thermometer, and a clock/watch or timer) to measure. This finding suggests that EWS may be feasible to implement in low-resource settings where more sophisticated monitoring and diagnostic equipment may be unavailable (Allegranzi & Pittet, 2007). However, evidence from a prospective cohort study identified the need for local validation and impact assessment of EWS tools before their adoption in resource-limited settings (Wheeler et al., 2013).

This systematic review provides more information than the previous systematic review in 2013 (Betesh et al, 2013), on the predictive accuracy and effectiveness of

obstetric EWS. Our results support the hypothesis that EWS may improve the quality of monitoring of obstetric patients, possibly resulting in improved reaction time by clinical staff to prevent further deterioration. These findings agree with outcome improvement reported with EWS in non-obstetric patient population (Alam et al., 2014).

To the best of our knowledge, this is the first systematic review to report predictive accuracy, and effectiveness on clinical outcomes of obstetric EWS. Other strengths of this review include adherence to the good practice of protocol registration and use of a robust tool for quality assessment in diagnostic accuracy studies. A limitation of our review is the lack of standardization of the defining criteria for outcomes. For instance, maternal morbidity was defined based on the CDC criteria in the study by Shields and colleagues (2016) while other studies (Austin et al., 2014; Singh A et al., 2016; Singh S et al, 2012) defined morbidity based on consensus among authors. We, therefore, identified a need to standardize outcomes in EWS effectiveness studies for clinical and research purposes. Most of the studies included were observational studies and only one of the studies that assessed the effectiveness of EWS in improving clinical outcomes had death as a primary outcome. More robust studies with large sample sizes are required to detect the effect of EWS on maternal deaths. There were different versions of obstetric EWS across hospitals in keeping with lack of standardization as reported for non-obstetric systems. (Alam et al., 2014) This can result in a lack of familiarity with local systems when staff move between clinical areas and hospitals.

Moreover, while excluding studies of qualitative methodological design has significantly eased our analysis and reporting of the synthesised evidence, we acknowledge the potential drawback of missing evidence on contextual factors that could affect implementation of EWS, hence a limitation of this review.

Finally, the 12 EWS validation studies revealed a strong association between high scores and adverse obstetric outcomes. However, only one study assessed the time interval between the EWS trigger across different parameters and intravenous antibiotic administration (Maguire et al., 2015). Robust studies, for example, cluster-

randomized controlled trials, with the interval between a trigger and corrective clinical action as an outcome measure, are needed.

2.10. Chapter summary

Chapter 2: Systematic literature review

- Using search terms that comprised a combination of text words and synonyms related to the intervention and outcomes of interest, primary studies on obstetric EWS published in peer-reviewed journals between January 1997 and March 2018 were sought.
- A total of 381 articles were retrieved from peer reviewed journals and grey literature, out of which 17 met the inclusion criteria.
- A narrative synthesis was conducted because the outcomes reported by the included articles were heterogeneous.
- All studies were conducted on participants that were applicable to the reviews research questions, and majority (11-14 studies) had low risk of bias for patient selection, index test and flow of participants based on QUADAS-2 quality assessment.
- Eleven studies evaluated the predictive accuracy of EWC, 5 studies assessed the effectiveness of EWS in improving clinical outcomes, while one study addressed both objectives.
- Sixteen EWC were reviewed, 14 of which included five basic clinical observations (pulse rate, respiratory rate, temperature, blood pressure, and consciousness level) that are routinely collected in resource limited settings, hence feasible to use in such settings.
- The identified charts had very high median (inter-quartile range) sensitivity - 89% (72% to 97%) and specificity - 85% (67% to 98%) but low median (inter-quartile range) positive predictive values - 41% (25% to 74%) for predicting morbidity or ICU admission.
- Obstetric EWS had a very high accuracy in predicting death (AUROC >0.80), and can significantly reduce the severity of obstetric morbidity.
- Obstetric EWS improves the frequency of routine vital sign observation and reduces the interval between observation of specifically defined abnormal clinical observations and corrective clinical action.

2.11. Conclusion

Obstetric EWS are highly sensitive and specific in predicting obstetric morbidity and ICU admission with relatively low, but comparatively acceptable PPV. This supports their utility as valuable bedside screening tools for morbidity among the general obstetric population. Early warning systems are highly accurate in predicting maternal death among critically ill obstetric patients, but there is limited evidence of their effectiveness in reducing maternal deaths. Obstetric EWS may improve the frequency of routine vital signs observation and may reduce the interval between patient deterioration and corrective clinical action. These can potentially improve the quality of care for pregnant/post-partum women and reduce the risk of adverse obstetric outcomes. Most obstetric EWS versions have basic clinical observations that can be routinely collected in resource-limited settings making them feasible for use in such settings. More robust studies are however needed to assess the effectiveness of obstetric EWS in reducing maternal deaths.

Chapter 3: Methodology

3.1. Overview of the chapter

To explore the current literature on the use of EWS in obstetric practice (objective 1), a systematic literature review was conducted. Methods used in the systematic review were presented in **Chapter 2**: Systematic literature review.

To assess feasibility and predict possible problems with the implementation of obstetric early warning charts in Nigeria (objective 2), a mixed-method (cross-sectional survey and qualitative interviews/focus group discussions (FGDs)) study design was employed. Design and internal validation of an obstetric EWS model and score-based chart for use in low-resource settings (objective 3) was achieved using a case control retrospective analysis of secondary data. A controlled quasi-experimental trial and qualitative interviews/FGDs were employed to externally validate (objective 4) and explore the experience and challenges of using the designed obstetric EWS (objective 5), respectively.

This chapter gives an overview of the methods used to achieve study objectives 2, 3, 4 and 5 and the details are exhaustively discussed under the relevant chapters. It begins with the definition of terms commonly used throughout the study. Next, the study settings and key characteristics are presented, and the data collection and analysis methods followed according to the study objectives. Finally, ethical issues considered in the study and a description of measures taken to ensure the integrity and quality of the data are provided.

3.2. Definition of key terms

Maternal morbidity

A WHO technical working group, the Maternal Morbidity Working Group (MMWG), defines maternal morbidity as *"any health condition attributed to and/or aggravated by pregnancy and childbirth that has a negative impact on the woman's well-being"* (Firoz et al., 2013). Classifications of maternal morbidities vary, but the

most common classification is based on severity, into non-life-threatening morbidity, and severe morbidity or near miss (defined below), and on duration into acute and chronic maternal morbidity (Firoz et al., 2013; Koblinsky et al, 2012).

Near miss

Near miss is related to maternal morbidity, as described above (**Section 1.3.1**), as the extreme of severe morbidity. It is also referred to as severe acute maternal morbidity (SAMM). However, considering that the term "maternal near miss" best reflects the concept of "nearly dying but surviving", the WHO working group on maternal mortality and morbidity classifications recommends the use of this term instead of SAMM. The WHO defines maternal near miss as *"a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy"* (Say, Souza, & Pattinson, 2009). A woman is therefore considered a near miss when she has survived a life-threatening condition defined based on clinical criteria related to the specific disease entity, intervention-based criteria, or criteria based on specific organ system dysfunctions (WHO, 2011; Say et al., 2009).

Maternal mortality

Maternal mortality is defined by the tenth revision of the International Classification of Diseases (ICD-10) as *"the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes"* (WHO, 2011).

Severe maternal outcome (SMO)

The Maternal Morbidity Working Group (MMWG), defines SMO as the occurrence of a life-threatening condition (i.e., organ dysfunction) resulting in maternal death or maternal near miss (WHO, 2011).

Post-partum haemorrhage (PPH)

The World Health Organization defines PPH as *"blood loss greater than or equal to 500ml within 24 hours after birth",* and severe primary PPH as *"blood loss greater than or equal to 1000ml within 24 hours"* (World Health Organization, 2015). Following a caesarean section, PPH has been defined as blood loss in excess of 1000ml (Pahlavan et al, 2001; WHO et al, 2015). These definitions are based on

quantification of blood loss originating from "historical" studies published in the early 1960s (Rath et al, 2011). PPH is classified as primary (within the first 24 hours of delivery) and secondary (more than 24 hours after delivery but less than 12 weeks).

Antepartum haemorrhage (APH)

APH is defined as *bleeding from the genital tract in the second half of pregnancy before birth of baby* (WHO, 2011). In approximately half of all women presenting with APH, a diagnosis of placental abruption (premature separation of normally situated placenta from the uterine wall) or placenta praevia (placenta that lies wholly or partly on the lower uterine segment) will be made; no firm diagnosis will be made in the other half even after investigations (APH of indeterminate origin) (Varouxaki, Gnanasambanthan, Datta, & Amokrane, 2018). Other less common causes of APH include vasa praevia (presence of unsupported fetal vessels below the fetal presenting part, where the cord insertion is velamentous) and bleeding from the lower genital tract (Varouxaki et al., 2018).

Abortion and stillbirth

The WHO defines abortion as *"termination of pregnancy by expulsion of embryo/fetus before 22 weeks of pregnancy or below 500 g of weight"*, and stillbirth as "*the birth of a baby at ≥ 22 weeks of gestation or with birth weight of ≥ 500 g or body length of ≥ 25cm who died before or during labour and birth"* (WHO, 2006). The legal requirements for the registration of fetal deaths and therefore the threshold to diagnose a stillbirth versus abortion vary from country to country and even within countries. For international comparisons, stillbirth has been defined as a baby born dead at ≥ 28 weeks of gestation, or birth weight of ≥ 1000 g, or a body length of ≥ 35cm (Frøen et al., 2011). In this thesis, the latter definition is used to distinguish abortion from stillbirths.

Ectopic pregnancy

Ectopic pregnancy is a condition in which the pregnancy implants in a location other than the uterine endometrium. While most ectopic pregnancies occur in the fallopian tube (up to 97%), pregnancies can also implant in the abdomen, cervix, ovary, and cornua of the uterus (Fay et al., 2017).

Obstructed labour

Obstructed labour is a disorder of feto-pelvic relationships characterized by failure to progress despite strong uterine contractions (Kongnyuy, 2008). It results from mechanical problems – a mismatch between fetal size, or, more accurately, the size of the presenting part of the fetus and the mother's pelvis, although some malpresentations, notably a brow presentation or a shoulder presentation (the latter in association with a transverse lie) will also cause obstruction (Neilson et al., 2003). Pathological enlargement of the fetal head, as in hydrocephalus, may also (though rarely) obstruct labour (Kongnyuy, 2008; Neilson et al., 2003).

Pregnancy-induced hypertension (PIH)

Hypertension in pregnancy generally refers to BP of 140/90 mm Hg or above. It is broken down into two categories of severity: mild–moderate (140 to 159/90 to 109 mm Hg) and severe (≥160/110 mm Hg) (ACOG, 2013). Four major hypertensive disorders in pregnancy have been described by the ACOG: 1) chronic hypertension; 2) pre-eclampsia/eclampsia; 3) chronic hypertension with superimposed pre-eclampsia; and 4) gestational hypertension (ACOG, 2013).

Chronic hypertension

Chronic hypertension is defined as BP of 140/90 or higher mm Hg that either predates pregnancy or develops before 20 weeks of gestation (ACOG, 2013). Chronic hypertension complicates 3.6% to 9.1% of pregnancies and is usually (88.8%) attributed to essential hypertension (Malha et al., 2018).

Pre-eclampsia and eclampsia

Pre-eclampsia is a pregnancy-specific syndrome that develops in the latter half of pregnancy, characterized by a de novo onset of hypertension (BP ≥ 140/90 mm Hg) after 20 weeks of gestation and, traditionally, proteinuria (>0.3 g per day) (Line Malha et al., 2018; WHO, 2011). More recently, it has been recognized that non-proteinuric forms of pre-eclampsia exist, and guidelines' diagnostic criteria for pre-eclampsia have been updated to include additional signs/symptoms: neurological symptoms, thrombocytopenia (platelets <100,000/µL), pulmonary oedema, raised transaminase enzymes (alanine aminotransferase (ALT), or aspartate aminotransferase (AST) above twice the normal range) and renal insufficiency (creatinine > 1.1 mg/dL or doubling) (ACOG, 2013b). In the absence of proteinuria,

a woman can still be diagnosed with pre-eclampsia if she has any of the above-listed signs/symptoms, assuming these findings cannot be attributed to another illness. Eclampsia complicates approximately 3% of cases of pre-eclampsia and is the occurrence of seizures that cannot be attributed to other causes (ACOG, 2013; Malha et al., 2018).

Chronic hypertension with superimposed pre-eclampsia

The diagnosis of superimposed pre-eclampsia is made in women with chronic hypertension if proteinuria or a severe feature of pre-eclampsia develops for the first time after 20 weeks, in association with an increase in BP (ACOG, 2013).

Gestational hypertension

Gestational hypertension is defined as high blood pressure (BP ≥ 140/90 mm Hg) developing after 20 weeks of gestation, not associated with the systemic features of pre-eclampsia (e.g., proteinuria) (ACOG, 2013). Some women (up to 25%) may ultimately develop signs of pre-eclampsia, so the final diagnosis of gestational hypertension can only be made post-partum.

Skilled birth attendant (SBA)

The WHO defines an SBA as an accredited health professional such as a midwife, doctor or nurse who has been educated and trained to proficiency in the skills needed to manage normal (uncomplicated) pregnancies, childbirth and the immediate postnatal period, and in the identification, management and referral of complications in women and newborns. (WHO, 2004)

Skilled birth attendance

Skilled birth attendance constitutes *"Skilled Birth Attendants working together within an enabling environment"* (WHO, 2004). Adequate skilled birth attendance during labour, delivery and the early post-partum period could prevent as many as 75% or more of maternal deaths (Donnay, 2000; Thadddeus and Maine, 1994). For this reason, the percentage of deliveries assisted by an SBA is used as a proxy indicator for reducing maternal mortality (AbouZahr & Wardlaw, 2001).

Low-income country:

A country with gross national income (GNI) per capita of $995 or less (World Bank, 2018).

Lower-middle-income country:

A country with GNI per capita between $996 and $3895 (World Bank, 2018).

Upper-middle-income country:

A country with GNI per capita between $3896 and 12,055 (World Bank, 2018).

High-income country:

A country with GNI per capita of $12,056 or more (World Bank, 2018).

3.3. Methods

3.3.1. Background of study location: Nigeria

Nigeria is the setting for this research. The country lies on the west coast of Africa between latitudes 4°16' and 13°53' north and longitudes 2°40' and 14°41' east. It occupies approximately 923,768 square kilometres of land stretching from the Gulf of Guinea on the Atlantic coast in the south to the fringes of the Sahara Desert in the north. The territorial boundaries are defined by the republics of Niger and Chad in the north, the Republic of Cameroon in the east, and the Republic of Benin in the west (**Figure 3.1**).

Figure 3 1 Map of Nigeria showing the 36 states and the surrounding countries

Nigeria is divided into 36 states and the capital city (FCT Abuja; **Figure 3.1**). These are regrouped into six geopolitical zones: North-east (with six states), North-west (with seven states), North-central (consisting of six states and the capital city), South-east (with five states), South-west (having six states) and South-south (consisting of six states). Each state is further subdivided into varying numbers of

autonomous local government areas (LGAs), with a total of 774 LGAs across the country (Federal Republic of Nigeria, 2016).

Nigeria has the largest economy in Africa, with a gross domestic product (GDP) greater than $500 billion, which grew steadily by over 7% per annum between 2005 and 2014, but this growth has been slower since 2015 (Federal Republic of Nigeria, 2016). The GNI per capita is approximately $2778, which places it as a lower-middle-income economy (World Bank GNI ranking 136) (World Bank, 2018). Health expenditure as a percentage of GDP is 3.56%, of which 72.2% is out of pocket (World Bank, 2017). The country's economic strength is derived largely from its oil and gas reserves, with agriculture contributing 39% of the total GDP (Demographic and Health Survey, 2013).

At the latest census in 2012, the total population of Nigeria was around 166.2 million, with an estimated annual population growth rate of 2.6% (National Bureau of Statistics, 2019). In 2016, the country was estimated to have over 178.5 million people, although United Nations projections have placed the population as high as 186 million (National Bureau of Statistics, 2018). The Nigerian population is predominantly young, with about 41% of the population being 15 years old or younger and has a median age of 18.4 years. The male-to-female ratio is approximately 1:1 throughout the population (National Bureau of Statistics, 2018).

Average life expectancy at birth is 54.5 years (WHO, 2016b). The total fertility rate has remained consistently high, though showing a slight downward trend from 5.7 births per woman in 2003–2008 to 5.5 births per woman by 2013 (Demographic and Health Survey, 2013). 23% of women aged 15–19 have already begun childbearing and about one third (32%) of women age 20–49 have given birth by age 18 (Demographic and Health Survey, 2013). There are substantial differences in fertility rates across the place of habitation, as rural areas tend to have higher fertility rates (average 6.2 births per woman) than urban areas, where the rate is about 4.7 births per woman. Similarly, there are large urban–rural differences in age-specific fertility rates (ASFRs) for all age groups. The largest variations are in the 15–19 and 20–24 age groups; in these groups, the rates for rural women exceed those for urban women by 100 and 79 births per 1000 women, respectively.

Adolescent fertility in rural areas is more than double that in urban areas (Demographic and Health Survey, 2013). The crude birth rate was 39 per 1000 (2013) (Demographic and Health Survey, 2013), and the death rate was 12.46 per 1000 (World Bank, 2016). Although several native languages are spoken by the Nigerian people, the official language is English; given this, all scoping activities in this research were conducted in the English language.

3.3.2. Maternal and child health (MCH) situation in Nigeria

Maternal morbidity and mortality

Just like many other sub-Saharan African countries, Nigeria has one of the poorest maternal and child health indices in the world. Complications due to pregnancy and childbirth constitute the principal causes of morbidity and mortality among women. In 2015, there were an estimated 814 maternal deaths per 100,000 live births, which approximates to 20% (one in five) of the 303,000 maternal deaths recorded globally (WHO Factsheet, 2016). Additionally, an estimated 1 million to 1.6 million Nigerian women suffer from serious disabilities/complications from pregnancy and childbirth-related causes annually (Abdul-wasi, 2017).

Like many similar countries in the sub-saharan Africa, vital registration in Nigeria is grossly inadequate, hence mortality indices derived based on model estimates (Alkema et al, 2016). This is even more pronounced in the Northern regions, where this research was conducted, a region having the highest MMR with estimated maternal mortality of more than 1000/100,000 live births in some of the states (Doctor et al, 2012; Guerier et al, 2013). A large country wide cross-sectional survey conducted across 1000 primary health care centres reported that most maternal deaths in this region occur at home (Ochejele S et al, 2019). For example, one of the states in this region, Kebbi state, has the worst reproductive health indices in Nigeria: more than two-third (71%) of pregnant women in the state never attended antenatal care; 91% of the women delivered at home; less than 10% had skilled birth attendance during the most recent birth, among others (Gulumbe U et al, 2018).

Use of MNH and EmOC services

Nigeria lags behind in terms of antenatal care (ANC) utilization. The 2014 World Health Statistics (WHO, 2014) reported that only 61% of pregnant women in Nigeria ever made at least one contact with a skilled ANC provider and only 57% made "at least four visits", as recommended by the WHO, between 2006 and 2013, despite the availability of free ANC in most parts of Nigeria (WHO, 2014).

Availability and utilization of EmOC in Nigeria has remained relatively stagnant over the last 10 years (Kabo, I.et al 2019). Childbirth attended by a skilled birth attendant and in a health care facility each increased by only three percentage points from 35% in 2003 to 38% in 2013 and from 33% in 2003 to 36% in 2013, respectively (NDHS, 2013). Births occurring at home decreased by only three percentage points during the 10-year period from 66% in 2003 to 63% in 2013 (NDHS 2013). Traditional birth attendants assist 22% of all deliveries, 23% of births are assisted by a relative or other person, and 13% are unassisted (NDHS, 2013). However, a more recent WHO estimate puts the skilled birth attendance rate at 43% (WHO, 2018b).

Similarly, findings of research in other developing countries have indicated poor utilization of EmOC among women who have experienced obstetric complications. In a study conducted in nine sub-Saharan African countries, researchers showed that only 28% of women who experienced obstetric complications obtained EmOC (Geleto A et al, 2018). In a recent study, it was indicated that the met need for emergency obstetric care was 22% (Miltenburg AS et al, 2017), while the met need of EmOC for Malawian and Zambian women was reported to be 20.7% (Kongnyuy EJ et al 2009) and 27% (Ng'anjo Phiri S, et al, 2016) respectively. In Ethiopia, the findings of Admasu et al. (2011) showed that only 6% of women who experienced obstetric complications were treated at health institutes (Ng'anjo Phiri S et al, 2016)

Places of birth, delayed presentation and determinants

Health facility delivery has been described as one of the major contributors to improved maternal and child health outcomes (Anoje C et al, 2012). It provides access to appropriate equipment and drugs, skilled attendants and immediate referral to a higher facility (UNICEF 2019). Proportions of health facility delivery vary across continents and regions. While 9 in every 10 births take place in health facility in Europe, Central and East Asia, the Pacific, Latin America and the Caribbean, only 56% of all births occur in health facility in sub-Saharan Africa (UNICEF 2019). This average performance in respect of facility delivery has reflected in the maternal mortality records in the region. As at 2015, maternal mortality rate in sub-Saharan Africa was 546 per 100,000 live births, accounting for 66% of the global maternal deaths (WHO 2018b; World Bank 2018; United Nations 2019).

Only 36% of births in Nigeria occurred in health facilities in 2013, as compared with 35% in 2008. The proportion of births occurring in health facilities decreased with increasing birth order, from a high of 48% for first births to a low of 22% for births of order six or above. Women in rural areas are more likely to deliver at home (77%) than their urban counterparts (37%). Similarly, women with higher levels of educational attainment were more likely to deliver in a health facility than women with less or no education. For example, women with more than secondary education (91%) were eight times as likely to deliver in a health facility as women with no education (11%). The proportion of births occurring in a health facility increased steadily with increasing wealth quintile, from 6% of births in the lowest quintile to 80% in the highest quintile (Demographic and Health Survey, 2013). The North-west had the highest proportion of births at home (88%), followed by the North-east (79%). The South-east had the lowest proportion of home births (20%), followed closely by the South-west (24 %) (Demographic and Health Survey, 2013).

Overall, the utilization of obstetric services in Nigeria is determined by various factors such as quality of care, cost of services, accessibility, socioeconomic status, female education, and traditional/religious sentiments (Ogunniyi et al, 2000; Igwebe et al, 2011). The attitude of health workers and the fee-for-service system have also been variously implicated (Onah et al, 2006; Igwebe et al, 2008). These

factors contribute to type 3 delays in the prevention of maternal mortality according to the model of Thaddeus and Maine (Thaddeus and Maine, 1994): a delay in management after arrival at the health facility. Type 1 delays occur when a pregnant woman fails to seek health care in time in the event of an obstetric emergency, and type 2 delays are related to difficulty with transportation. This delay model provided the framework for the needs assessment conducted by the Society of Gynaecology and Obstetrics of Nigeria (SOGON) in the 6 geopolitical zones in Nigeria, which implicated type 3 delays as the major contributor to the high MMR in the country (Igwebe et al, 2008).

Child health indices

It is also estimated that Nigeria had 104.3 under-five deaths per 1000 live births in 2016 (WHO, 2018b). The neonatal and infant mortality rates were 37 and 69 per 1000 live births respectively; the under-five mortality rate had declined by 31%, and the infant mortality rate by 26% over the last 15 years (WHO, 2018b). At this mortality level, nevertheless, one in every 15 Nigerian children dies before reaching the age of one, and one in every eight does not survive to their fifth birthday.

Progress on MCH targets

Overall, Nigeria could not meet the maternal and child health (MCH) targets of the MDGs 4 and 5 by 2015; however, appreciable progress has been made in this area (**Table 3.1**), and there is a strong commitment to greater improvement in the post-2015 SDG era (Abdul-wasi, 2017). The establishment of government interventions, such as the Petroleum Subsidy Re-investment and Empowerment Program for Maternal and Child Health (SURE-PMCH) initiative to incentivize uptake of maternal and child health services; the Global Polio Initiative; and the Immunization Strategic Plan are all strong measures put in place to accelerate progress towards achieving the ambitious SDG MCH targets (Abdul-wasi, 2017).

Table 3 1 MDGs 4 and 5 indicators achievement for Nigeria

MDGS			1990	2015
Goal	**Target**	**Indicator**	**Estimate**	**Target (actual)**
Goal 4: reduce child mortality	Reduce by two-thirds between 1990 and 2015 the under-five mortality rate	4.1 <5 mortality rate/1000	191	64 (81)
		4.2 Infant mortality rate/1000	91	31 (58)
		4.3 Proportion of 1-year-old children immunised against measles (%)	54	>90 (42)
Goal 5: Improve maternal health	**Target 5A:** Reduce by three quarters, between 1990 and 2015, the maternal mortality ratio	5.1. MMR/100, 00 live births	1350	450 (814)
		5.2. The proportion of birth attended by skilled health personnel (%)	30.8	(35)
	Target 5B: Achieve by 2015, universal access to reproductive health	5.3. Contraceptive prevalence rate	6.0	(20.4)
		5.4. Adolescent birth rate/1000 women	148.0	(111.2)
		5.5. ANC coverage, At least 1 visit	56.5	(65.8)
		At least 4 visits	52	(49.1)
		5.6. unmet needs for family planning	21.5	(21.9)

Source (United Nations, 2015; WHO Factsheet, 2016; Abdul-wasi, 2017; World Bank, 2017e, 2017b, 2017a, 2017c; UNICEF, 2018)

3.3.3. The organization of the Nigerian healthcare system

The Nigerian health system includes orthodox, alternative and traditional systems of healthcare delivery regulated by the government (WHO, 2008). The orthodox system constituting mainstream healthcare is provided by the public and private sectors. The public healthcare system is organized into primary, secondary and tertiary healthcare levels. The federal government is responsible for policy development, regulation, overall stewardship, and providing healthcare at the tertiary level (teaching hospitals and specialist hospitals). The state governments are responsible for secondary healthcare, while the LGAs manage primary healthcare (PharmAccess Foundation, 2014). The LGA level is the least-funded and -organized level of government and therefore has not been able to properly finance and organize primary healthcare, creating a very weak base for the healthcare system (PharmAccess Foundation, 2014). Consequently, the referral system between the three healthcare levels is not always respected because the two lower

levels, especially the primary level, are very weak, with inadequate infrastructure, personnel and other deficiencies (PharmAccess Foundation, 2014).

The 2005 Federal Ministry of Health's (FMOH) census reported an estimated total of 23,640 health facilities, of which 85.8% were primary healthcare facilities, 14% secondary and 0.2% tertiary; around 9000 health facilities belonged to the private sector, which provided at least 70% of healthcare services in the country (PharmAccess Foundation, 2014). On average, private healthcare costs more than public healthcare, and private facilities are better managed in terms of structure and other resources than public health facilities. In order to improve healthcare infrastructure, the federal and state governments are adopting a public–private partnership strategy; multiple models are being used in Nigeria, but the most common is the arrangement in which government solely finances the infrastructure and contracts a private entity to operate the facility (PharmAccess Foundation, 2014).

Overall in 2014, there were 134,000 hospital beds across the country, which approximates to 0.8 beds per 1000 population, which is well below the rate for the African region (USDC, 2016 in PharmAccess Foundation 2014). There is gross inequity in the distribution of health facilities to the disadvantage of rural areas and northern parts of the country. There are more hospitals in the western part of the country as compared to the other regions; fewest hospitals (in terms of the type and quality of healthcare services) are situated in the northern part of Nigeria, a region with the worst health indices (PharmAccess Foundation, 2014).

3.3.4. Human resources for health (HRH)

Apart from south-western Nigeria, which alone accounts for 43.9% of the medical doctors and the majority of the other health workers, there is a general shortage of HRH in the rest of the country (International Organization for Migration, 2014). Acknowledging this, the Nigerian National Strategic Health Development Plan (NSHDP) 2009–2015 stated that *"there is a dearth in the quality, quantity and mix of health care workers with a skewed distribution towards urban and southern population, alongside the existence of multiple categories of health care providers from orthodox to traditional"* (NHRHISS, 2012). The most recent estimate states

that Nigeria had 4.0 physicians and 16.1 nursing/midwifery personnel per 10,000 populations. This puts the total HRH density (physicians, nurses and midwives) at 20.1 per 10,000 population, which is less than the African average of 22, and the WHO recommendation of 23 doctors, nurses and midwives per 10,000 population (WHO 2017; WHO, 2018).

The North-east zone is the hardest hit by shortages in HRH, followed by the North-west. **Table 3.2** shows that the North-east, with 14% of Nigeria's population, has only 4% of its doctors, whereas the South-west, home to 20% of the population, has 43.9% of the doctors. The North-west, more populous than the South-west and with a higher disease burden, has only one fifth of the country's doctors. Most of the country's medical doctors are concentrated in the tertiary and secondary health facilities located in urban areas (International Organization for Migration, 2014).

Table 3 2 Regional distribution of Nigeria's health workers in percentages

Categories of HRH	Total un-updated stock	North-central Percentage	North-east Percentage	North-west Percentage	South-east Percentage	South-south Percentage	South-west Percentage
Physicians	**52 408**	**9.73**	**4.06**	**8.59**	**19.59**	**14.37**	**43.9**
Nurses	128 918	16.40	11.65	13.52	15.29	27.75	15.35
Radiographers	840	14.30	3.66	5.97	1500	18.30	43.00
Pharmacists	13 199	19.94	3.80	7.79	11.74	12.39	44.00
Physiotherapists	1 473	10.08	2.73	8.32	8.58	7.93	62.00
Medical Laboratory Scientists	12 703	6.82	1.72	3.6	35.26	23.89	62.00
Environment and public health workers	4 280	9.39	11.27	18.94	12.36	15.69	32.08
Health Records officers	1 187	13.34	4.85	11.6	14.64	29.90	26.00
Dental Technologists	505	14.08	5.92	5.92	12.96	16.62	44.50
Dental Therapists	1 102	13.19	10.29	21.88	10.19	12.99	31.50
Pharmacy Technician	5 483	7.17	9.12	18.00	8.58	11.80	46.00
Percentage of Nigeria's population	100	***14***	14	26	12	15	20

(Source: AHWO, WHO and the European Union, 2008, p.23, cited by International Organization for Migration, 2014)

Worthy of note, however, is the absence of an up-to-date database for the actual Nigerian health workforce. For instance, there were 39,210 Nigerian doctors on the medical register in 2005, which grew to 52,408 in December 2007 and 55,376 in 2008; however, only 14,000 doctors (27% of the reported stock) had paid the

annual practising licensing fee for the year 2007. The same applies to all other medical professions and no register has ever been updated to take into account the number of deaths, retirement, migration or any other form of exit (International Organization for Migration, 2014). This has created a visible disconnect between the number and mix of health workers and the country's needs on the one hand and, on the other, available health facilities (World Bank, 2013). This, in turn, blinds the country to the glaring gaps in health resources. To this end, the Federal Ministry of Health, in collaboration with the World Health Organization and the United States government, commenced the establishment of the National Human Resources for Health Information System (NHRHIS) in 2010 (NHRHISS, 2012). The system is expected to, among other things, capture the information of new graduates from different health institutions annually and to present summary statistics based on a number of human resources for health indicators, which will present Nigeria's human resources for health status in relation to local and international benchmarks (NHRHISS, 2012). Sadly, however, no data have yet been produced by the NHRHISS.

3.3.5. Human resource for Maternal Health

Distribution of human resource for maternal care is greatly influenced by the presence of tertiary hospitals, social amenities, and a population that can afford to pay for health services (Abimbola S, et al 2012). Additionally, obstetric specialty training happens in tertiary healthcare centres, most of which are situated in urban areas. This in turn attract highly skilled obstetricians and midwives to more affluent settings (Abimbola S, et al 2012). Therefore, in much of rural Nigeria, beyond issues of access, there are inadequate human resources for providing 24-hour health services, especially the basic essential obstetric care, in primary health care (PHC) facilities (Koblinsky M et al, 2016).

Efforts to better reach underserved communities, most of which are in the north, have been on task shifting to community health workers (CHWs) (Samb B et al, 2007). While task shifting has offered a cost-effective expansion of the overall HRH pool, skilled attendance at birth is essential to reducing the burden of maternal mortality (Campbel OM 2006). The shortage of skilled birth attendants in rural

Nigeria impacts negatively on utilisation of services by women in these areas (Koblisky M et al, 2006).

Launched in December 2009, the Midwives Service Scheme (MSS) was set up to address the HRH needs, especially for MNH services, in rural primary care, based on the evidence that when the number of midwives increases, utilisation of services increases, women's satisfaction with care improves, and maternal and newborn mortality decrease (Campbel OM et al, 2006; Betran AP et al, 2005). To do this, three categories of midwives were recruited as part of the MSS: the newly graduated, the unemployed, and the retired. They are posted for 1 year (renewable subject to satisfactory performance) to selected PHCs in rural communities.

The facilities selected for the MSS were linked in an effective two-way referral system through a cluster model in which four PHC facilities with the capacity to provide basic essential obstetric care were clustered around a general hospital with the capacity to provide comprehensive emergency obstetric care. There were 815 participating health facilities: 652 PHC facilities and 163 general hospitals. Each PHC facility has four midwives to ensure 24-hour provision of skilled birth attendance at all times, as well as other maternal and child health services (Abimbola S et al, 2012).

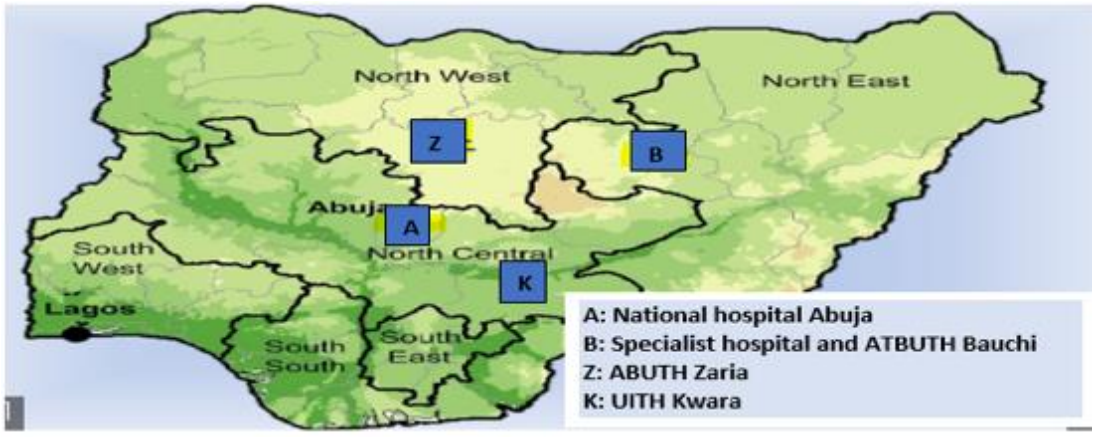
3.3.6. Study sites and sampling method

In selecting the study area and facilities to be included in this research, the focus was on northern Nigeria, where health indices, including the burden of adverse obstetric outcomes, are poorest. It was critical that we recruited a representative sample of health facilities through randomization to ensure generalizability of our findings across this region. However, a huge logistical challenge was foreseen if random sampling were to be employed across the 19 northern states. Given this, the decision was made to recruit facilities based on purposive sampling, but ensuring as much diversity and representation as was feasible. While this was the case in phase 1 (feasibility study) and phase 3 (implementation and evaluation of EWS) control sites, which required primary data, the second phase (design and internal validation of the obstetric EWS model for use in low-resource settings) used representative secondary data on women with severe maternal outcome (SMO)

collected previously across 42 Nigerian tertiary hospitals (Oladapo et al., 2016); details of this phase are discussed in **Chapter 5**. Selection of phase 3 intervention site was based on convenience sampling. The University of Ilorin Teaching Hospital (UITH) was a new implementation site in a new phase of CMNH's Johnson & Johnson's grant (charity number 222655) project for improving the quality of care of maternal and newborn health (MNH) in Kwara state, Nigeria. CMNH had not implemented any quality improvement intervention at UITH prior to phase 3, when this study was conducted.

A total of five health facilities were selected- 4 were sampled purposively (and one based on convenience) from the three geopolitical zones of northern Nigeria (**Figure 3.2**). The selected facilities were National Hospital Abuja (NHA); Bauchi State Specialist Hospital; Abubakar Tafawa Balewa University Teaching Hospital (ATBUTH), Bauchi; Ahmadu Bello University Teaching Hospital (ABUTH), Zaria and University of Ilorin Teaching Hospital (UITH), Kwara.

Figure 3 2 Map of Nigeria showing the five selected health facilities



The selected hospitals were tertiary healthcare facilities providing comprehensive emergency obstetric care (CEmOC). **Table 3.3** gives a regional distribution of these hospitals and the relevant research phases that each facility was recruited for.

Table 3 3 Study sites (health facilities) for the three research phases

Health facility	Level of care	Region	Study phase included
ABUTH Zaria	Tertiary	North-west	1* and 2*
Specialist Bauchi	Tertiary	North-east	1
NHA Abuja	Tertiary	North-central	1, 2 and 3*
ATBUTH Bauchi	Tertiary	North-east	2 and 3
UITH Kwara	Tertiary	North-central	3

*1: feasibility study, *2: design and internal validation phase, *3: external validation phase

3.3.7. Rationale for sampling study sites

The five tertiary hospitals sampled for this Ph.D. were selected across 3 geo-political zones of northern Nigeria, where burden of preventable maternal morbidity and mortality is highest (IOM 2018, Koce et al, 2019). Selection of tertiary healthcare facilities is informed by the fact that about 60 to 90% of patients reportedly bypass the lower level facilities to self-refer to the tertiary referral hospitals in Nigeria (Aguwa et al, 2010; Okoli et al, 2017). The indiscriminate use of the higher levels of care has led to the lower level facilities in Nigeria becoming underutilised and unrecognised, thus, wasting the resources and skills of the healthcare providers serving those facilities (Koce et al, 2019), and potentially unsuitable for inclusion into this research. Moreover, there is a significant skewness in the distribution of HRH in favour of the tertiary facilities, with resultant higher turnover of patients (IOM, 2018). This has been attributed to the less attractive remuneration and inferior work conditions in the lower level health facilities (IOM, 2018). However, we do acknowledge the resulting lack of generalizability of our findings (especially the feasibility and implementation phases (one and three)) to secondary and primary healthcare facilities. This has been listed under study limitations in the last chapter (chapter 7) of this thesis.

3.3.8. Study design and data collection

This research employed a mixed methodology consisting of cross-sectional surveys, reviews of secondary records, direct non-participant observations, case-control retrospective analysis of secondary data, qualitative key informant interviews (KII)

and focus group discussions (FGDs). The research design and data collection methods used depended on the research questions addressed by the specific objectives of the three research phases.

The feasibility study was conducted in three tertiary hospitals, one in each of the geopolitical zones of the north (**Table 3.3**). We employed a mixed-method (quantitative and qualitative) research design to achieve the phase's objectives.

Design and internal validation of the obstetric EWS model and score-based chart for use in low-resource settings was conducted using secondary data on 5360 obstetric admissions from across 42 Nigerian tertiary hospitals. This phase was achieved using a quantitative (case-control) study design.

In the last phase, the proposed chart was implemented and externally validated using a mixed-method research design consisting of a controlled quasi-experimental quantitative component and qualitative interviews and FGDs. One teaching hospital (University of Ilorin Teaching Hospital) was used as the intervention site and two other teaching hospitals (Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, and Abubakar Tafawa Balewa University Teaching Hospital (ATBUTH), Bauchi) were recruited as control facilities.

Table 3.4 gives an overview of the data collection methods used; data collection was undertaken by the principal researcher, assisted by research assistants in all study sites. Participation in the research was absolutely voluntary. No financial incentive was given to participants; details of recruitment of participants, data collection tools and methods are discussed in the relevant chapters of this thesis (chapters 4, 5 and 6 for phases 1, 2 and 3 respectively)

Table 3 4 Overview of the research design and data collection methods

Study phase	Objectives	Study design	Data collection methods
Phase one *Feasibility study*	To obtain information needed for sample size calculation for phase 3 of the research.	Cross-sectional survey/ review of secondary records	Review of registers and summary sheets in labour wards, lying-in wards, ANC wards, obstetric wards and High Dependency or Intensive Care Units (HDU/ICU) between 1st August 2016 and 31st July 2017
	To explore in-patient monitoring of pregnant or recently pregnant women with complications in Nigerian Hospitals	Qualitative study design	KIIs, FGDs and non-participant observation of nurses, midwives and doctors.
	To Identify potential challenges to use of obstetric early warning chart and how these may be remedied to make use of the chart feasible.	Qualitative study design	KIIs, FGDs and non-participant observation of nurses, midwives and doctors.
	To explore the acceptability of early warning system for maternal monitoring and opinions of healthcare staff regarding the chart	Qualitative study design	KIIs, FGDs and non-participant observation of nurses, midwives and doctors.
Phase 2 *Design and internal validation of EWS model and score-based chart*	To design and use robust statistical methods to internally validate a simple EWS model for use in resource-limited settings.	Quantitative (case-control) study design	Retrospective analysis of secondary data
	To assess effectiveness of obstetric early warning chart in improving measured patient outcomes	Quantitative (controlled quasi-experimental) trial	Review of secondary records for baseline patient characteristics and EWS parameters pre-implementation (1st August to 31st October 2018),

			then prospective data collection of same parameters post-implementation (1ST December to 31st March 2019).
Phase 3 *Implementation and external validation*	To explore experience and challenges of using the chart among health care providers	Qualitative study design	KIIs, and FGDs with nurses, midwives and doctors

3.3.9. Ethical considerations

As with all ideal research studies involving human subjects, the four fundamental principles of bioethics stated in the Belmont report (Beauchamp, 2008), namely the principles of autonomy, non-maleficence, beneficence and justice, formed the basic ethical foundation on which this research was conducted.

Additionally, the Principle of Respect for Dignity and the Principle of Veracity, to include elements of patient care and medical decision-making that are not explicitly covered by the original four principles (Snyder et al, 2008), were strictly adhered to. All efforts were put in place to uphold the dignity of participants, and to preserve anonymity, confidentiality, and protection against psychological harm. The strategies through which these were achieved during data collection, management and storage are described in the following subsections.

Ethical consideration for data collection

To collect data used for this research, ethical approvals were received from the Research and Ethics Committee of the LSTM. Separate approvals were sought and granted for the feasibility study (Research Protocol 17-47: Approval in **Annex 3A**), and the implementation/external validation phases (Research Protocol 18-074: Approval in **Annex 3B**), which were prospective studies requiring primary data. Following provisional approval from LSTM, we applied for and were granted in-country approvals by the three feasibility study sites (**Annexes 3C1–C3**) for phase 1, and the intervention and control sites (**Annexes 3D1–D3**) for phase 3, before full ethical approvals were granted.

For phase 2, which required secondary data, clearance was obtained from the principal investigators of the Nigerian Near-miss study (from the WHO, Geneva, Switzerland) for the use of the data. A data use agreement was signed, in which the Principal Investigators indicated that the analysis was covered under the approved use of data by the Ethics Review Committees both at the WHO and in all 42 participating hospitals. However, additional approval for the analysis (ethics waiver) was obtained from the Research Ethics Committee of LSTM (Protocol ID 17-047).

Potential adverse effects, discomforts and risks that participants might experience during this research were identified:

1. The qualitative research activities included non-participant/direct observation of healthcare workers (in phase 1). Some participants may, therefore, feel uncomfortable being observed or may tend to overract because of their awareness of being observed (Hawthorne effect).
2. Interviewees and participants of FGDs may have a problem in taking time off work to participate in the study.
3. Conducting FGDs could disturb members of the public who seek care from the health workers.
4. Some FGD participants may need to discuss personal or confidential information and may feel uncomfortable doing so in the midst of their superiors.
5. There is a potential risk of coercion of participants into the study.
6. For phase 3, evidence already exists for the usefulness of early warning charts. It could therefore be argued that having control sites will deny the participants at the control sites of the benefit of the intervention.

Steps taken to minimize these adverse effects, discomfort and risks to the participants were as follows:

a. Participants were reassured that no evaluation or judgement of their practice would be drawn from the observation. To adjust for the Hawthorne effect, we audited records of previous shifts preceding the date of observations and used these to triangulate with the findings of the direct observation.
b. All participants were made aware of the fact that they did not have to respond to any questions that they felt were personal or if answering them made them feel uncomfortable.
c. We minimized the ethical challenge of participants taking time off work by being flexible with the timings of KIIs and FGDs to meet the needs of research participants. We conducted FGDs at times when they would interfere the least with the routine daily activities of participants. The principal researcher received advice from the participants' line managers on this. Adequate notice was given to participants so they had time to prepare.

d. Regarding denying control participants the benefits of the intervention, this was minimized by collecting only secondary data at the control sites. We also plan to disseminate our findings to the two control sites and possibly introduce the charts afterwards at the earliest available opportunity.

e. Overall, participation in all research activities was entirely voluntary, and participants had the opportunity to withdraw from the study at any time. Any participant who agreed to participate in the research was provided with an information sheet and an informed consent form (**Annex 3C**), which detailed the purpose of the research, participant expectations, the procedure of the enquiry (different procedure for FGDs and KIIs), potential risks and discomfort, and privacy and confidentiality. Only participants from whom informed consent had been obtained were included in the study.

f. The WHO Research Ethics Review Committee template for informed consent was used for this research (attached as appendices to the relevant thesis chapters). The informed consent form had two parts: information sheet and certificate of consent.

   The information sheet contained the following information: name of principal investigator, name of organization, name of sponsor, name of project, purpose of the research, type of research intervention, reasons for participant's selection, voluntary participation, details of the research procedure, expected duration required to complete the questionnaire, KIIs or FGDs (depending on participant), potential risks and benefits of the study, and assured confidentiality of the research.

   For FGDs, in which confidentiality was harder to achieve, participants were told that members of the group would be asked not to discuss the talk with people outside, but it was stated that this could not be guaranteed.

g. Only necessary information was collected from participants. The research assistants were trained on data collection to ensure data quality and integrity of research ethics. Full names of participants were not requested, but participant names were coded, their roles stated and anonymity maintained.

Ethical consideration for data management

All secondary data were used only within the boundaries of the agreement guiding its use. Secondary data for phase 2 were secured on the principal researcher's password-protected computer, to ensure that there were no data leaks or unauthorized use of data.

For FGD and KII data, data analysis and presentation remained anonymous to ensure that no specific individual could be identified and to prevent any unfortunate consequences of participating in the FGDs or KIIs. All the collected data were kept strictly confidential. All field notes and transcripts were also secured in a locked drawer, accessible only to the principal researcher and research assistants.

Ethical considerations for data storage

The laptop containing all data was password-protected, and only the principal researcher knew the password. No other person apart from the principal researcher had access to the computer files that contained the data collected.

Also, data were stored with non-identifiable coded names (understood only by the principal researcher) on the computer as second-line protection. Data are being stored securely with password protection for the five-year period, after which they will be destroyed, following LSTM's guidelines on data security.

Data were not stored in any online/cloud storage, to safeguard the data and ensure that no other person will have access to it.

3.3.10. Quality control

The term quality control refers to *"the efforts and procedures that researchers put in place to ensure the quality and accuracy of data being collected using the methodologies chosen for a particular study"* (Roe, 2008). Quality control was maintained throughout the research, by monitoring of the process, both for the quantitative and qualitative components of the research. The strategies I employed to achieve this monitoring process include the following:

First, a robust quality assessment tool (Quality Assessment of Diagnostic Accuracy Studies: QUADAS-2) was employed to scrutinize the studies included in the

systematic review. Details of how this was achieved were presented previously (**Chapter 2**: Systematic literature review).

For the review of secondary records in phase 1 and secondary data used in the case-control analysis in phase 2, double entry was employed to ensure data quality; analysis in phase 2 was undertaken by two researchers (the principal researcher and an independent statistician) using two separate statistical software platforms. Details of these are discussed in the relevant chapters (Chapters 4 and 5).

In the quasi-experimental trial (phase 3), compliance was audited by the principal researcher and the local implementation team (consisting of three doctors and one senior nurse (chief nursing officer in charge of the obstetric and gynaecology emergency unit) in the intervention study site) during the immediate post-implementation period daily for two weeks to ensure that the chart was being correctly used for all eligible participants. Subsequently, monthly audits were performed by the implementation team (in consultation with the principal researcher via Skype/telephone calls) to monitor the use of the chart and any ongoing change in practice. A quality assessment checklist was adopted from the work of Merriel and colleagues (2017) (tool attached as an appendix to **Chapter 6**) to provide the implementation team with a simple way to achieve the quality audits. Specific details of the surveillance and monthly audit results are presented in **Chapter 6**.

For the FGDs and KIIs, a comprehensive and detailed standardized operating procedure manual, which aligns with the phase-specific research protocols, guided all data collection. Topic guides were pretested before use in the full KIIs and FGDs and only asked relevant questions and avoided redundancy to ensure data efficiency.

Emphasis was placed on the trustworthiness of the research. We ensured that participants felt comfortable and that they were able to express themselves and behave naturally (credibility); this was achieved by ensuring that sufficient rapport was established between the researcher and the researched. Efforts were made to ensure that the samples were representative of the study population and data collection continued up to the point when no new information was being retrieved

during the FGDs and KIIs (i.e., saturation was achieved). In addition, key findings collected from the focus groups were repeated to the participants to verify that they recognized them, and that their intended meaning was conveyed (confirmability).

All these quality control activities were put in place to ensure data quality and thus improve the credibility of our findings.

3.3.11. Data management and analysis

Quantitative data

All data were managed in accordance with the Liverpool School of Tropical Medicine's (LSTM) policy on data management. They will be stored for a maximum of five years and will be destroyed afterwards. Quantitative data collected were entered into a computer and cleaned before analysis. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 25 and/or Stata version 15.1. Summaries were calculated for each facility, and/ or study arm (intervention and control sites for phase 3) where appropriate. Characteristics of the study population were summarized by means and standard deviations for continuous variables and percentages for categorical variables. Continuous variables were compared through analysis of variance or Kruskal-Wallis tests, depending on whether variables were normally distributed or not. Normality was assessed visually through distribution plots and with the Shapiro-Wilk test. Frequency tables and charts were used to present simple proportions and trends. We constructed 95% confidence intervals (95% CI) for all performance characteristics. Statistical significance was determined at a p-value <0.05. Details of analysis specific to each research phase are presented in the relevant chapters of this thesis (chapters 4, 5 and 6 for phases 1, 2 and 3 respectively).

Qualitative data

All FGDs and KIIs audio scripts from phases 1 and 3 were independently transcribed verbatim. The transcripts were analysed using a thematic framework approach. This method was chosen because of its systematic approach to data management and its emphasis on transparency in the analysis (Richie et al, 2003).

Familiarization was carried out by repeated listening to the audio recordings. Transcripts were imported to computer-assisted qualitative data analysis software

(CAQDAS; NVivo 11). Data were explored using NVivo query commands, and thoroughly reviewed to identify the important themes and concepts, and these were appropriately coded. The codes were sorted and grouped under a smaller number of broader categories of main themes and placed within an overall thematic framework.

The framework was subsequently indexed into the raw data to check how categories fitted in. Missing categories were added to the framework and appropriately labelled. Data were sorted by themes and subsequently reduced through summarization and synthesis (Richie, J., Spencer, L., 2003). Sets of thematic matrices were created and each main theme with its associated subtopics was plotted on a separate thematic chart. Respondents were allocated rows in the matrix and subtopics were displayed in separate columns. Key parts of the data were summarized and placed appropriately in the thematic matrix. Throughout the charting process, an attempt was made to achieve a balance between reducing the data and preserving the context and the language in which it was expressed.

After completing the data management steps, we tried to make sense out of the evidence synthesized using descriptive accounts (Richie, J., Spencer, L., 2003). Results were presented using different NVivo data presentation tools including charts, tree maps and graphs.

3.4. Chapter summary

Chapter 3: Methodology

- An overview of the methods used to achieve study objectives 2, 3, 4 and 5 was presented in the methodology chapter
- Methods for objective 1 (literature review) were presented in **Chapter 2**: Systematic literature review, while details of the methods used to achieve the remaining objectives are exhaustively discussed under the relevant thesis chapters (chapters 4, 5 and 6 for objectives 2, 3 and 4/5 respectively).
- The study was predominantly conducted in northern Nigeria. Purposively selected facilities for this research were considered representative of the three geopolitical zones of this region.
- Ethical principles guiding biomedical research were strictly adhered to, throughout this research.
- Ethical approvals for primary data collection were obtained from LSTM and Nigeria (from all study sites). Use of secondary data was approved by custodians for the data in WHO and Nigerian hospitals with an ethics waiver from LSTM.
- Mixed research methods (qualitative and quantitative) were used for data collection: primary data from healthcare workers (nurses, midwives and doctors) and secondary data from review of medical records.
- Quantitative data were collected using cross-sectional surveys, case-control study of previously collected research data, and prospective data from a controlled quasi-experimental trial. Data were analysed with SPSS version 25 and Stata version 15.1 statistical software.
- Qualitative data were collected using direct observation, focus group discussions and key informant interviews with healthcare workers (nurses, midwives and doctors). The thematic framework approach was used to analyse qualitative data.
- Quality assurance and quality control systems were implemented throughout the study to ensure data quality.

Chapter 4: Feasibility study

4.1. Overview of the chapter

This chapter presents formative research conducted to investigate the feasibility of use of obstetric EWS in selected Nigerian tertiary hospitals. The chapter starts by providing the rationale for this study, then the study objectives, study design and data collection methods used are presented. Thereafter, the ethical considerations specific to this phase are described, as well as the quality assurance steps implemented. Data management and analysis are described, and the chapter concludes by presenting and discussing the main findings of the feasibility study.

4.2. Rationale

Sufficient evidence on the usefulness of obstetric EWS was established, based on an already completed systematic literature review, conducted as part of this research (presented in **Chapter 2**: Systematic literature review). The findings from this review strongly supported the usefulness of EWS both as triaging tools and in improving quality of care and health outcomes. The review also provided evidence supporting the feasibility of use of EWS in low-resource settings with the potential to contribute to a reduction in maternal morbidity and mortality (Umar, A., et al*.,* 2019). However, the performance of EWS has been shown to vary significantly with setting. In a prospective cohort study, charts developed in well-resourced settings were found to perform poorly in a resource-limited setting (Wheeler et al., 2013). Specifically, the evidence showed loss of both sensitivity and specificity of the adopted EWS tools, and a context-specific score that addressed challenges peculiar to the local population showed a much-enhanced accuracy (Wheeler et al., 2013). This underscores the need to understand potential challenges associated with the introduction of EWS across all contexts. Such baseline feasibility assessment may contribute to context-specific adaptations to improve effectiveness.

4.3. Aim and objectives

The aim of this phase of the PhD research was to assess the feasibility of implementation of obstetric EWS in Nigerian hospitals.

The specific objectives were as follows:

1. To explore inpatient monitoring of pregnant or recently pregnant women with complications by non-participant observation.
2. To identify potential challenges associated with the use of obstetric EWS non-participant observation and analysis of secondary data, and to recommend remedial measures to increase the feasibility of using EWS in a low-resource setting.
3. To explore the acceptability of EWS by maternity care providers and the opinions of healthcare staff concerning its use, using key informant interviews and focus group discussions.
4. To obtain information needed for sample size calculation and design of phase 3 of the PhD research, by secondary data analysis.

A mixed (quantitative and qualitative) study design was employed to achieve these objectives. Among the most important contributions of qualitative methods to research programmes in the development phases are provision of data on feasibility, generation and refinement of hypotheses, and prediction of problems with implementation (Richie, J., Spencer, L., 2003). Hence, the main objectives of the feasibility study (objectives 1, 2 and 3) were achieved using qualitative research design (direct non-participant observations, key informant interviews (KII) and focus group discussions (FGDs)). To obtain the baseline information needed for sample size estimation and design of the subsequent phases of the project (objective 4), a cross-sectional survey was used.

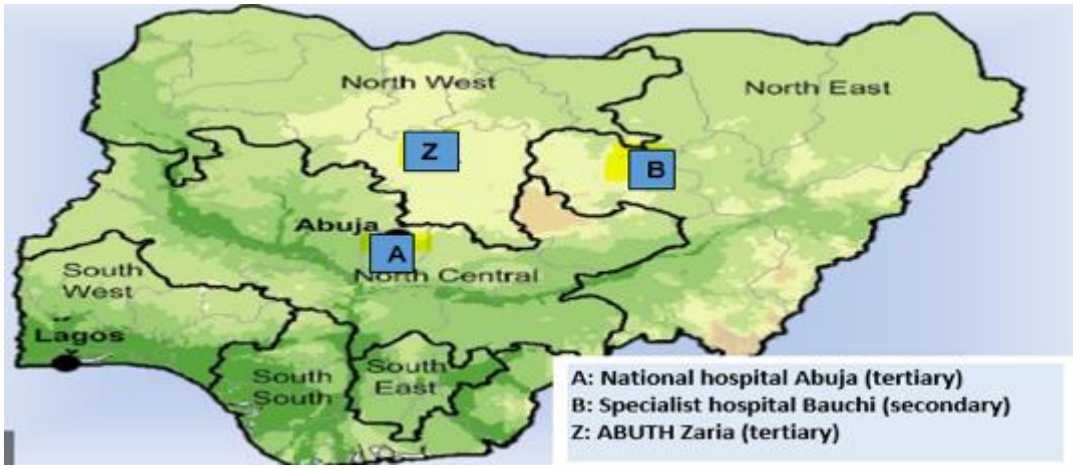
4.4. Methods

4.4.1. Study settings

The settings for the feasibility study were three tertiary hospitals: Ahmadu Bello University Teaching Hospital (ABUTH) Zaria, National Hospital Abuja (NHA) and Bauchi State Specialist Hospital. All are CEmOC facilities that were selected using purposive sampling across the North-east (Specialist Hospital Bauchi), North-central (NHA) and North-west (ABUTH) geopolitical zones of northern Nigeria (**Figure 4.1**), where the MMR is significantly higher than the national average

(Demographic and Health Survey, 2013; National Population Commission, 2019). Background characteristics including health indices of these settings were presented previously (**Chapter 3**: Methodology).

Figure 4 1 Map of Nigeria showing the feasibility study sites



4.4.2. Quantitative methodology and data collection

A cross-sectional survey was used to collect the information required for the sample size estimate and design of phase 3. The research questions to be addressed were as follows:

1) What is the prevalence of the proposed phase 3 outcome measures (obstetric morbidity and mortality)?

2) How many eligible participants would be available at the potential facilities?

Questionnaires were designed (Supplementary file: **Annex 4A**) and used to collect secondary data from various secondary sources (**Table 4.1**) that answer these questions in each facility. The variables included the recorded number of maternal deaths, near misses, birth rate, modes of delivery and the range and volume of obstetric morbidity seen in the related hospitals.

Data were collected for 12 months preceding the date of the feasibility study (from 1st August 2016 to 31st July 2017), to calculate annual incidence and period prevalence rates. This task was undertaken by the principal researcher assisted by research assistants from each of the three study sites. **Table 4.1** gives a brief description of the variables collected using a specially designed secondary data collection tool.

Table 4 1 Description of the survey data collection tool

S/no	Variable	Description of variable	Source of data
1	Number of births	Total number of births in the facility every month for 12 months	Registers and summary sheets in labour wards, lying-in wards, antenatal wards, obstetric wards and high-dependency or intensive care units (HDU/ICU)
2	Mode of childbirth	Number of births by mode of delivery every month for 12 months	
3	Incidence of obstetric complications	Incidence of obstetric complications as defined by healthcare providers every month for 12 months	
5	Number of maternal deaths	Total number of maternal deaths as recorded by healthcare providers every month for 12 months	

4.4.3. Qualitative methodology

Key informant interviews (KII) and focus group discussions (FGDs) were conducted to explore maternal healthcare monitoring practices, views of healthcare staff on obstetric early warning systems and potential challenges with EWS implementation. KIIs targeted purposively selected but experienced midwives and nurses in administrative positions who had the potential to provide relevant information to address the study objectives. The inclusion criteria that guided the sampling of nurses/midwives were as follows:

i. Had at least five years of clinical experience in maternity.
ii. Had an additional administrative role.

Medical doctors were purposively sampled and included in the KIIs with a view to exploring contextual factors from their perspectives. Doctors across different levels including interns, registrars and consultants working in the obstetric units of the feasibility study sites were interviewed. The reasons KII was considered most appropriate for these categories of participants were, first, that it provided an opportunity to have one-to-one in-depth discussions with experienced participants about their perceptions of EWS as an innovation in their places of work, and possible challenges with implementation, and an opportunity to obtain useful suggestions regarding the design and use of the chart in maternal monitoring and

care; and second, that it was more practical to set up KIIs with these individuals at their convenience rather than FGDs (Marshall, 1996).

FGDs were conducted with junior nurses and midwives who undertook monitoring of women on admission in the included wards. By targeting these participants for FGDs, we aimed to explore and understand exactly how monitoring, trigger and response would work and understand the limitations to optimal functioning from the viewpoint of those providing these services (Richie et al*.,* 2003). More widely used in qualitative research (Richie et al., 2003), non-probability/purposive sampling was used to select staff undertaking maternal monitoring tasks in the selected wards who fulfilled the following inclusion criteria to be invited to FGDs:

i. At least one year of clinical work experience in maternity obstetric/ANC/lying-in wards or critical care units.

ii. Must be in active clinical practice (not in administrative positions only).

A list of all eligible FGD participants was made from duty rosters and staff profiles. From this list, focus groups were constituted such that all the wards were evenly represented.

Potential participants for the KIIs and FGDs were contacted through either direct contact, SMS or telephone calls at least one week prior to the proposed date of data collection. Details of the purpose of the study and proposed format of the interview or FGD (face-to-face, phone or Skype calls) were explained to them. Participant information sheets (**Annex 4B**), a sample of the coloured MEOWS chart used in Liverpool Women's Hospital, and consent forms were given to all participants, after which data collection sessions were arranged with those who verbally consented based on their convenience. Participation was entirely voluntary. No financial incentive was given to the participants.

4.4.4. Qualitative data collection

Data collection tools

Topic guides were developed in English for the KIIs and FGDs. While the same FGD topic guide was used throughout, different KII topic guides were used for doctors, and for nurses and midwives. Background information on characteristics of respondents, including coded identification number, cadre, rank, wards, duration

of clinical and maternity experience, and proportion of time spent on clinical and administrative roles, was collected on a separate KII/FGD log (**Annex 4C**). The topic guides (**Annexes 4D and 4E**) discussed the clinical tasks undertaken by the respondents, vital signs monitoring and how this varied under different patient circumstances, the process of triggering a response to abnormal findings and how this was escalated to clinicians of different levels of expertise. Next, the topic guides asked about management of trigger events by nurses and doctors, and their opinions about EWS. Anticipated challenges and suggestions were discussed particularly using the KII topic guides.

Key informant interviews

The KIIs were facilitated by the principal researcher, who had received qualitative research training. Given this, he could create an optimal environment for interacting with the interviewee. Before the start of each KII session, the facilitator read the informed consent form to participants, checked their willingness to participate and recorded it on the consent form, and recorded relevant information in the KII log. All participants consented to audio-recording of the interviews. All interviews were recorded with parallel note-taking of important points. Both copies of the consent form handed out to each participant at the beginning of the interview were signed: one copy was given to the participant, while the other was kept in the research file.

All KIIs with nurses and midwives were held in their respective offices, while doctors were interviewed via Skype calls from the principal researcher's base in Liverpool, UK. Overall, interview sessions lasted 45 to 60 minutes. During all interview sessions, the interviewer asked the interviewee questions and awaited their response, without directing the conversation. Transcription was done soon after data collection, and the recording, transcription and notes made were used in the data analysis.

Focus group discussions

FGDs were held with junior nurses and midwives who routinely undertook the tasks of monitoring obstetric inpatients in the included facilities. By conducting the FGD, we aim to explore and understand exactly how monitoring, trigger and response works and understand the limitations to optimal functioning from view point of

those providing this service. Areas of practice covered during the feasibility study were antenatal care, labour ward including lying-in wards, postnatal medical and postnatal surgical ward. For these groups of participants, it was relatively easy to co-opt them to attend the discussions. The principal researcher and research assistants who facilitated the FGD sessions were all trained on how to moderate sessions. They had previous experience in conducting qualitative research and were able to facilitate an optimum environment for the interaction of focus group participants.

After participants were identified and the discussion groups constituted, participant information sheets were handed out. These sheets included details on the purpose and format of the session and stated that it would be recorded with permission of participants. Although financial incentives were not given to participants, light refreshments were provided after the FGD sessions. All participants consented to audio-recording of the FGD sessions. All FGD sessions were recorded and had parallel note-taking of important points. Both copies of the consent form handed out to participants at the beginning of the FGD sessions were signed. One signed copy was given to the respective participant, while the other was kept in the research file.

Having been provided with a copy of the MEOWS chart prior to commencement of the FGDs, participants were taken through one or two practical case scenarios of patient monitoring using MEOWS for clarity (Stewart et al, 2014), before getting them to discuss anticipated challenges and opinions on its perceived usefulness. FGD sessions lasted between 60 and 90 minutes. Transcription was done soon after data collection by a private transcription services provider, following which the principal researcher edited the transcripts for grammatical and typographical errors. This was done to increase the readability of the transcripts while maintaining the character of the participants' comments (Stewart et al, 2014). The recordings, field notes and transcripts were all used for data analysis.

Direct observation

Direct observation was added to the methodology of this phase with a view to expanding on and scrutinizing the findings of the KIIs, FGDs and structured

questionnaires (Richie, J., Spencer, L., 2003). The observation checklist used (**Appendix 4F**) consisted of the number of admissions during the shift, number of items of functioning patient monitoring equipment, average turnaround time for baseline investigations, and frequency of monitoring of vital signs (temperature, pulse rate, respiratory rate, blood pressure and SPO2). Vital signs charts and partographs completed during the previous shifts were also cross-examined for triangulation. Field notes were taken on staff's clinical skills for patient monitoring, including track and trigger and management of trigger events.

The observation was carried out by the principal researcher for a period of four days in each of the three research sites. The wards observed were the maternity, lying-in, antenatal and intensive care units. Observations were made between the hours of 9.00 am and 5.00 pm each day so that staff performing all three clinical shifts in the day were observed.

The observation data were used to corroborate the findings that emerged from the survey, KIIs and FGDs (Richie J., Spencer L., 2003). The data generated was mainly used in the write-up to corroborate and illuminate discussion of the findings drawn from the other data collection methods. In places where this is done, it is explicitly indicated that the observation has been used.

4.4.5. Data management and analysis

Quantitative data analysis

Data were entered into Microsoft Excel and cleaned. Double entry was employed to minimize error. Summaries were calculated for each facility. Frequency tables and charts were used to present simple proportions and trends. Comparison between continuous variables was done using means, while percentages were used to compare categorical variables. Period prevalence of maternal deaths, intensive care unit (ICU) admissions and different types of complications were calculated across feasibility study sites. Findings were presented in tables and charts and reported according to the research questions answered.

Qualitative data analysis

A thematic framework approach was employed to analyse qualitative data, following a verbatim transcription of interviews and FGD audio scripts. This method

was chosen because of its systematic approach to data management and its emphasis on transparency in the analysis (Richie, J., et al., 2006). The approach focuses on detecting and describing both implicit and explicit ideas (themes) within the transcripts. We followed Braun and Clarke's six-step method: familiarization, generating initial codes, searching for themes, reviewing themes, defining and naming themes, and producing the report (Braun & Clarke, 2006).

Familiarization was carried out by repeated listening to the audio recordings. Transcripts were imported to computer-assisted qualitative data analysis software (CAQDAS; NVivo 11). Data were explored using NVivo query commands, and thoroughly reviewed to identify the important themes and concepts, and these were appropriately coded. The codes were sorted and grouped under a smaller number of broader categories of main themes and placed within an overall thematic framework.

The framework was subsequently indexed into the raw data to check how categories fitted in. Missing categories were added to the framework and appropriately labelled. Data were sorted by themes and subsequently reduced through summarization and synthesis (Richie, J., et al., 2003). Sets of thematic matrices were created and each main theme with its associated subtopics was plotted on a separate thematic chart. Respondents were allocated rows in the matrix and subtopics were displayed in separate columns. Key parts of the data were summarized and placed appropriately in the thematic matrix. Throughout the charting process, an attempt was made to achieve a balance between reducing the data and preserving the context and the language in which it was expressed.

Having finished the data management steps, we tried to make sense out of the synthesized evidence using descriptive accounts (Richie, J., Spencer, L., 2003). Results were presented using different NVivo data presentation tools including charts, tree maps and graphs.

4.5. Ethical considerations and limitations

The LSTM Research Ethics Committee approved the research protocol for this study (17-047). The Research Ethics Committee of the Bauchi State Specialist Hospital, National Hospital Abuja and Ahmadu Bello University Teaching Hospital Zaria,

Nigeria, granted approvals at the local levels. Copies of approvals were attached as appendices to **Chapter 3** (Methodology) of this thesis.

General considerations for ethics throughout data collection, management, storage and analysis, including measures taken to ensure data quality, were described in detail previously (**Chapter 3**: Methodology). Additionally, however, the methodology adopted for the feasibility study has the following specific limitations, and therefore some strategies were developed to minimize their impact.

- For direct observation, the researcher took the role of non-participant observer and all observed staff were fully aware of the research. This may have led some participants to change their behaviour because they were being watched (Hawthorne effect). To minimize this, records of previous shifts were reviewed to triangulate findings from direct observation.
- It was not feasible to convene more than one focus group discussion per facility due to a shortage of staff capacity. The FGD topic guides were therefore not saturated at each facility. However, the focus group participants were similar in characteristics (**Table 3.3**) despite the heterogeneity of the three facilities. Also, the same topic guides were used for the FGDs in all sites. It could, therefore, be argued that the facilities can be taken as a single entity for FGD analysis. When this was done, all topics in the FGD topic guide were saturated by the three FGDs, hence addressing this potential major limitation.

4.6. Findings and discussion

The ensuing sections presents findings from the two methodological approaches employed in the feasibility study as follows:

- quantitative method (review of secondary records)
- qualitative methods (KIIs, FGDs and observation).

4.6.1. Findings from review of secondary records

During the 12 months (1st August 2016 to 31st July 2017) reviewed, a total of 5254 live births and 269 stillbirths were recorded in the three facilities, placing the overall live birth rate (LBR) and stillbirth rate (SBR) at 95.1% and 48.7/1000 births respectively. SBR is similar in the two teaching hospitals at 31 and 35 per 1000 births

(in NHA Abuja and ABUTH Zaria, respectively), but twice as much in the specialist (non-teaching) hospital (**Table 4.2**).

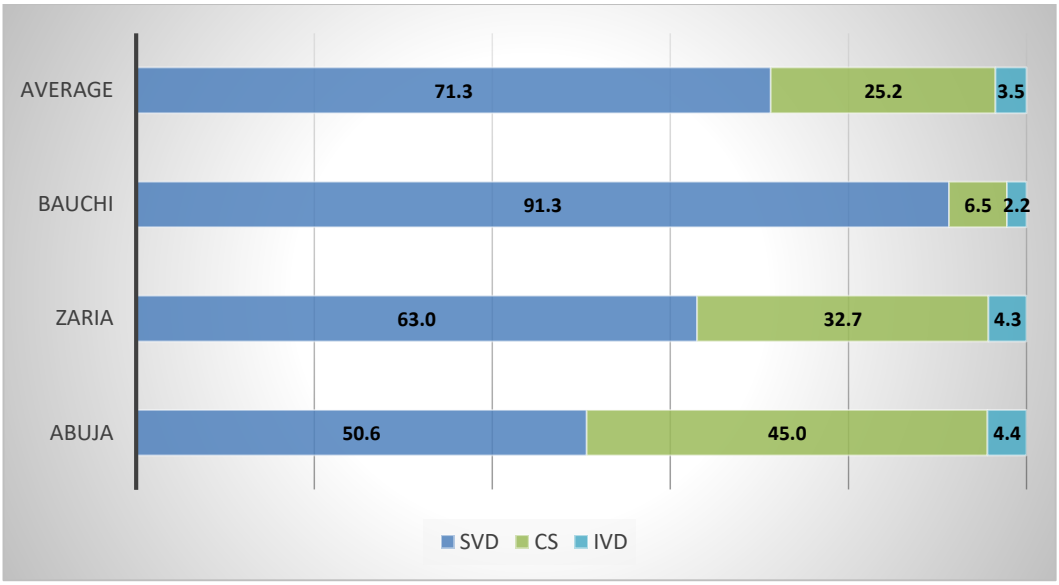
Table 4 2 Characteristics of the three feasibility study sites

Study site	Admissions	SBR /1000	PBR /1000	SVD (%)	CS (%)	IVD (%)
ABUTH Zaria	1930	38.3	82	63	32.7	4.3
NHA Abuja	1510	34.2	130	50.6	45.0	4.4
Specialist Bauchi	2362	73.6	75	91.3	6.5	2.2
Overall	5802	48.7	96	71.3	25.2	3.5

PBR: preterm birth rate; SBR: still birth rate; SVD: spontaneous vaginal delivery; CS: Caesarean section; IVD: instrumental vaginal delivery

Overall, Specialist Hospital Bauchi recorded the highest number of births at 2362, compared to National Hospital Abuja, which had the lowest (1510). Over 70% of all births were spontaneous vaginal, 3.5% were instrumental (vacuum or forceps), while overall caesarean section (C/S) rate in the three facilities was 25.2% (16.1% and 9.1% for emergency and elective C/S respectively; **Table 4.2** and **Figure 3.2**). Unlike with vaginal births, however, the two teaching hospitals had manifold higher C/S rates compared to Specialist Hospital Bauchi (**Figure 4.2**).

Figure 4 2 Modes of births (%) in the three study sites



Research question: what is the prevalence of the intended outcome measures (maternal deaths and maternal near misses)?

Monthly summaries were obtained for maternal deaths. There were no records of maternal near misses based on WHO near-miss criteria in any of the three facilities. Records were obtained for the intensive care unit (ICU) admissions of obstetric cases, and monthly summaries of different categories of obstetric complications as defined by the healthcare service providers.

During the 12-month period, 64 women died from pregnancy and childbirth in the three facilities, placing the estimated maternal mortality ratio (MMR) at 1218 per 100,000 live births. The estimated MMR varies across facilities, with Specialist Hospital Bauchi having the highest at 1376.4 per 100,000 live births. Abuja and Zaria had estimated MMR of 1075 and 1138.4 per 100,000 live births, respectively. However, no formal statistical testing was conducted between the facilities as the absolute number of deaths recorded was relatively small, so the inter-facility difference may be statistically insignificant (**Table 4.3**).

Table 4 3 Maternal deaths and ICU admissions in the three feasibility study sites

Study site	ICU admissions	ICU AR (%)	Maternal deaths	MMR /100,000 LB
ABUTH Zaria	52	2.7	21	1138.4

NHA Abuja	46	3.0	14	1075.0
Specialist Bauchi	-	-	29	1376.4
Overall	98	2.8	64	1218.1

ICU AR: intensive care unit admission rate; LB: live births

3% (n=46) of obstetric admissions in NHA Abuja were to the ICU, of which about 26% (n=12) died. ICU admission rate was slightly lower in Zaria at 2.7% (n=52) of obstetric admissions, with mortality rate of 31% (n=16). Specialist Hospital Bauchi had no functioning intensive care unit, and no records were available for high-dependency or intensive care admissions. However, the maternity complex had a four-bedded room for nursing eclampsia patients and other categories of patients diagnosed with severe obstetric complications (observation findings).

Overall, 22.6% of all obstetric admissions were complicated by at least one of four major complications: obstetric haemorrhage, hypertensive disorders, sepsis, and prolonged/obstructed labour (**Table 4.4**). 15.5% of all vaginal deliveries were either complicated by some degree of perineal tear, or the mothers required and were offered episiotomy (**Table 4.4**).

Table 4 4 Prevalence of obstetric complications by health facility

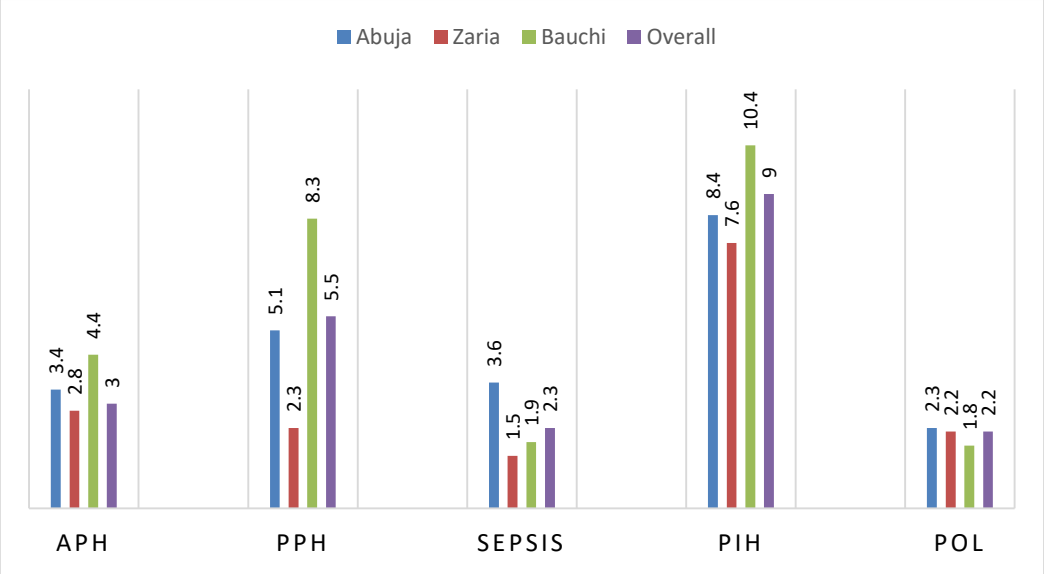
Complication	**Abuja (%)**	**Zaria (%)**	**Bauchi (%)**	**Total (%)**
Haemorrhage	128 (8.5)	98 (5.1)	300 (12.7)	526 (9.1)
APH	51 (3.4)	54 (2.8)	105 (4.4)	210 (3.0)
PPH	77 (5.1)	44 (2.3)	195 (8.3)	316 (5.5)
Hypertensive disorders	127 (8.4)	147 (7.6)	246 (10.4)	520 (9.0)
Gest. hypertension	37 (2.4)	43 (2.2)	71 (3.0)	151 (2.6)
Pre-eclampsia	61 (4.0)	71 (3.7)	119 (5.0)	251 (4.4)
Eclampsia	29 (1.9)	33 (1.7)	56 (2.4)	118 (2.0)
Sepsis	54 (3.6)	35 (1.5)	47 (1.9)	136 (2.3)
Prolonged/obstructed labour	35 (2.3)	42 (2.2)	43 (1.8)	120 (2.2)
Tear/episiotomy	403 (26.7)	376 (19.5)	437 (18.5)	1216 (21.0)

PPH: post-partum haemorrhage; APH: antepartum haemorrhage; denominator for deaths is LB, while for all others it is obstetric admissions.

The most frequent groups of complications were obstetric haemorrhage and hypertensive disorders, accounting for 9.1% and 9.0% of obstetric admissions

respectively (**Table 4.4**). In terms of specific disease conditions, post-partum haemorrhage was the most frequent, followed by pre-eclampsia, antepartum haemorrhage, gestational hypertension, sepsis, prolonged/obstructed labour and eclampsia in descending order. Post-partum haemorrhage (PPH) accounted for nearly a quarter of all obstetric complications recorded, and twice as many complications that resulted from eclampsia (**Table 4.4**). **Figure 4.3** shows the relative incidence of the different categories of obstetric complications at the facility level.

Figure 4 3 Incidence of obstetric complications (%) by health facility



POL: prolonged/obstructed labour; PIH: pregnancy-induced hypertension

The three hospitals admitted 5802 women for childbirth or complications of pregnancy over the 12-week period of this review. The average (SD) numbers of monthly obstetric admissions were 161 (25), 129 (18) and 197 (28) in Zaria, Abuja and Bauchi respectively. These represent the potentially eligible participants for entry to phase 3 of the PhD project. Using this and the prevalence of the intended outcome measures, the sample size, appropriate study design and expected recruitment time for participants to phase 3 (implementation and evaluation of EWS) were estimated in consultation with a statistician.

4.6.2. Qualitative results and main findings

Background

In total, 20 KIIs were conducted across the three data collection sites (seven, nine and four KIIs in Abuja, Zaria, and Bauchi respectively) (**Table 4.5**). Ten of the key informants were registered nurse-midwives holding ordinary nursing certificates. The remaining KIIs were conducted with clinicians including consultants (three), senior registrars (two), registrars (three) and interns (two).

The nurse-midwives were comparable across the three sites in terms of rank and the proportion of time spent doing administrative work (% admin work in **Table 4.5**). However, there exists a significant difference in work experience among nurse-midwives across study sites. In terms of both overall clinical experience and experience working in maternity, the participants in Specialist Hospital Bauchi were

significantly more experienced. Among those interviewed in the two teaching hospitals, the clinical experience of those from Zaria was higher, while participants from Abuja had more experience working in maternity (**Table 4.5**).

On the other hand, fewer medical doctors were interviewed in Specialist Hospital Bauchi (2 KIIs) compared to the two teaching hospitals (4 KIIs each) (**Table 4.5**). KII participants included a consultant obstetrician and an obstetric registrar (or equivalent medical officer) in all three hospitals. Additionally, a senior registrar and an intern (house officer) were interviewed in each of the two teaching hospitals. However, as Specialist Hospital Bauchi is a non-teaching tertiary hospital, no senior registrar or house officer (intern) was available for interview there (**Table 4.5**).

Table 4 5 Characteristics of KII participants

Facility	No. of KIIs	Gender	Participants	Admin work mean (%)	Rank
BAUCH	2	2F	Nurses	25	2 CNOs
	2	M/F	Doctors	N/A	Consultant and MO
ABUJA	3	F	Nurses	25	One CNO and 2 ACNOs
	4	3 M 1F	Doctors	N/A	Consultant, registrar, SR and HO
ZARIA	5	5F	Nurses	28	4 CNOs and 1 SNO
	4	5F	Doctors	N/A	Consultant, registrar, SR and HO

CNO: chief nursing officer; ACNO: assistant chief nursing officer; SNO: senior nursing officer; SR: senior obstetric registrar; HO: house officer (intern) M- Male F- Female

Three FGDs (one per facility) were conducted. A total of 20 nurses/midwives participated; of these, 12 (60%) were registered nurse-midwives with general nursing certificates, five (25%) had bachelor's degrees in nursing sciences, while only three (15%) were primarily midwives. **Table 4.6** describes the characteristics of the focus group participants.

Table 4 6 Characteristics of FGD participants

Facility	Participants (Gender)	Qualification	Clinical experience (range) in years	Maternity experience (range) in years	Admin work mean (%)
Bauchi	6F	4 RNMs 2 midwives	3–13	1–4	4
Abuja	6F	4 BSc 2 RNM	6–9	2–6.5	4
Zaria	8F	6 RNM 2 BSc	4.5–11	1–8	13

BNSC: bachelor's degree in nursing sciences; RNM: registered nurse-midwives F- Female

Labelling of quotations

In the course of presenting the qualitative findings, quotations will bear the identity number of respondents as assigned to them during data collection. This is anonymised, but abbreviations used are; KII N- key informant interview respondents from NHA Abuja, KII A- key informant interview respondents from ABU Zaria, KII B- key informant interview respondents from Bauchi Specialists Hospital, FGD A- focus group discussion participant from ABU Zaria, FGD N- focus group discussion participant from NHA Abuja, FGD B- focus group discussion participant from Bauchi Specialists Hospital.

Main findings

The semi-structured KII and FGD topic guides explored the following key sections of the research objectives:

a) Maternal monitoring practices in the feasibility study sites
(Research question: How is maternal monitoring performed in the feasibility study sites?)

b) Perceptions of health workers of obstetric EWS and its acceptability
(Research question: What is the perception of health workers of EWS and its acceptability?)

c) Potential challenges to EWS and how to address them
(Research question: What potential challenges could affect EWS implementation and what are the possible solutions?)

d) Suggestions on the design of early warning charts for use in resource-limited settings

(Research question: What are the suggestions regarding EWS design and implementation?)

These encompass the four research questions that the qualitative scoping activities answered. Hence, findings are presented in the ensuing subsections based on the four research questions.

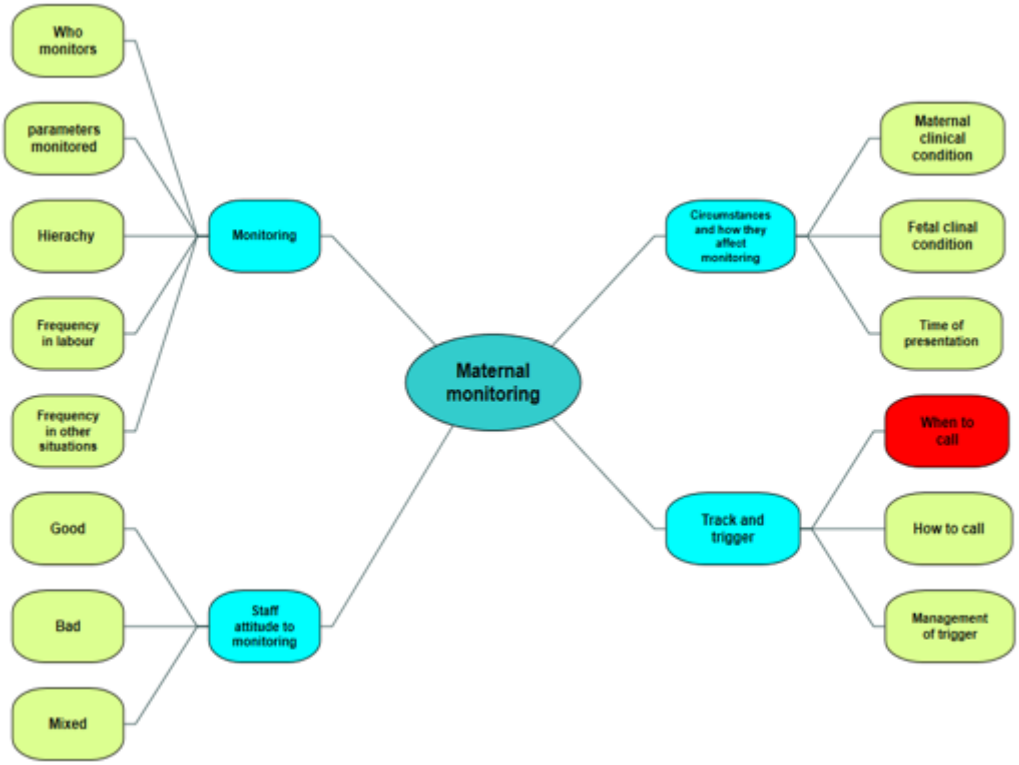
The transcripts were first explored to gain a preliminary understanding of the concepts using NVivo word frequency queries (**Figure 4.4**). Maternal monitoring, women, nurse, patients and vital signs were the most frequent words in the data, as illustrated in the word cloud (**Figure 4.4**).

Figure 4 4 Word frequency query (word cloud) of interviews and FGD transcripts

Research question: How is maternal monitoring performed in the feasibility study sites?

A maternal monitoring anchor code was created to explore monitoring practices in the transcripts. Four main themes emerged; these were monitoring and caregiving, circumstances affecting monitoring pattern, staff attitude to monitoring and track and trigger. Additionally, several related subthemes emerged. The main themes and their corresponding subthemes are illustrated in the mind map below (**Figure 4.5**). Summary tables of outputs of the thematic analysis of these themes conducted using NVivo 11, including a description of the main themes, frequencies of the relevant subthemes (nodes) and evidence from selected quotes, are provided as annexes (**Annexes 4F1–4**).

Figure 4 5 Visual map of themes relating to maternal monitoring practices



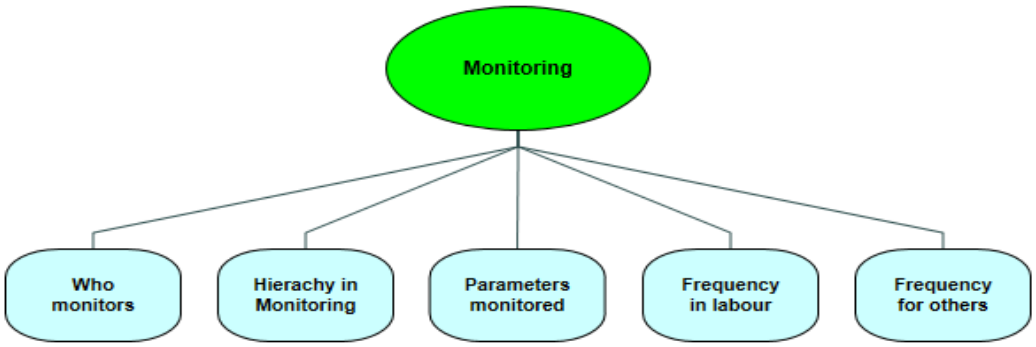
Theme 1: Monitoring

Subtheme 1.1: Who monitors?

Tasks of maternal monitoring, including monitoring of vital signs of women in labour, sick pregnant women, recently delivered women and those with puerperal complications, were undertaken by nurses and midwives. Although these are not their primary responsibilities, doctors also took part in patient monitoring in all the hospitals studied, as illustrated by the following quote from a senior nurse interviewee:

> *"…It's essentially nurses and midwives' work. Then the doctors do, HOs do. Doctors do at their level that is if they have patients on augmentation or when they're doing ward rounds, they monitor vital signs too. So, it's a combined effort really (KII NO3)"*

Figure 4 6 Monitoring and subthemes



Subtheme 1.2: Hierarchy in monitoring

Although midwives and nurses should have adequate training to assess and monitor uncomplicated births independently, there was a variation of roles according to rank and experience among nurses and midwives across all study sites. The following quote from a nurse key informant elucidates this finding:

> *"… There are some cases that when you see, the junior ones (meaning the junior/inexperienced midwives) know that they might not be able to handle those issues, so the senior ones will have to come in. you know… (KII A01)"*

Some roles, such as vaginal examination for cervical dilatation, fetal presentation, stations and features of obstruction, yielded more reliable findings when performed by experienced midwives. Nurses and midwives newly posted to relevant hospital wards were often made to work under supervision before they could undertake such tasks independently. Duty rosters were therefore made to ensure a senior person would be available on each shift to oversee the junior staff (direct observation finding). The following quotes from the matrons in charge of the labour wards of the two teaching hospitals affirmed this finding:

> *...everybody does but sometimes we try to prioritize some roles to the more experienced hands… (KII N02)*
>
> *"…even if they do it, when I come back I must cross-check, because like I said, I don't believe in your vaginal examination findings, because what you said is 3cm, 4cm might end up for me just 1.5cm (KII A05).*

Subtheme 1.3: Parameters monitored

In terms of the parameters routinely monitored, temperature, pulse rate, respiration and blood pressure were monitored in all categories of patients. In addition, urine output and analysis, fetal heart rate, uterine contractions and examinations of the vagina and gravid uterus were routinely performed in sick pregnant women and women in labour. In the tertiary centres, cardiotocographs (CTG monitors) were available for more convenient monitoring of fetal heartbeats, and digital monitors with SPO2 machines were used to monitor oxygen saturation (observation).

Subtheme 1.4: Monitoring frequency

Frequency of monitoring of vital signs varied with the diagnosis and clinical condition of the patients. There was a disagreement between nurses in the key informant interviews and focus group participants regarding this. While findings from KIIs revealed more frequent vital signs checks, FGD participants reported the contrary. Findings from observation were used to corroborate these discrepancies. For women in labour, the fetal heart rate was checked every 30 minutes, while blood pressure and temperature were monitored four-hourly. The frequency of vaginal examination (VE) depended on cervical dilation: if the patient's cervix was 1 cm to 6 cm dilated, the VE would be repeated every four hours, if 7 cm, VE would be repeated after three hours, if 8 cm, VE would be repeated after two hours, and if 9 cm, VE was repeated after one hour (observation). The following quote of a chief nursing officer from the specialist hospital illustrate this.

> *"…It is expected that she is supposed to dilate by a cm every hour, and that is why the VE depends on the cervical dilatation of the patient (KII B02)"*

Urinalysis was done for all women in labour at admission, and then daily for those with the hypertensive disease in pregnancy (observation). While this was often the case in the two teaching hospitals, vital signs monitoring was generally less frequent in the non-teaching tertiary (specialist) hospital. A nurse FGD participant with 12 years' overall work experience and five years' maternity work experience acknowledged this in the following quote, which also agrees with our findings from the non-participant observation:

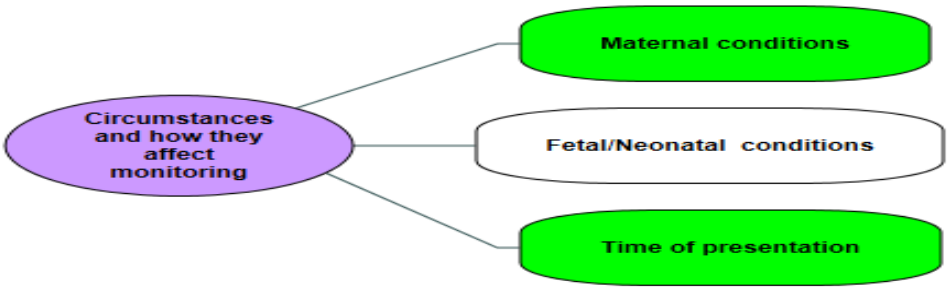
> *"…When the situation warrants you to take the vitals you take, but for you to say I will be monitoring vitals quarter hourly, half hourly or every hour, that is not possible here to be honest. Every two hours may be manageable, we do vitals two hourly when necessary, for all the vitals- the fetal heart rate, respiratory rate, pulse rate blood pressure and temperature…. (FGD B06)"*

The number and frequency of vital signs monitoring were variable. For stable patients in all three hospitals, vital signs were taken twice in 24 hours (6 am and 6 pm, observation). However, the monitoring pattern can be affected by different circumstances, which are discussed under the relevant theme in this chapter.

Theme 2: Circumstances and how they affect monitoring

The changes in monitoring pattern and associated circumstances were explored under the following themes (**Figure 4.7**).

Figure 4 7 Themes related to circumstances affecting monitoring



Subtheme 2.1: Maternal condition

Generally, findings of abnormal vital signs across all study sites lead to increased frequency of monitoring afterwards. The majority of the participants identified haemorrhage, hypertensive disorders of pregnancy, sepsis/pyrexia, poor progress of labour and altered level of consciousness as the most common maternal clinical conditions requiring close monitoring. There was no guideline on how these conditions affect vital signs monitoring in any of the hospitals visited. This is therefore determined at the discretion of nurses/midwives, unless specified by doctors. The following comments of two FGD nurses and a senior KII midwife

illustrate these points:

> *"…We do not have a strict guideline that we follow, but as a rule, whenever we feel concerned, we monitor more frequently…(KII N03)*
> *"…When you have a patient that is bleeding, then you definitely need to be your toes… (FGD B05)*
> *"…Usually, the doctors would let us know how often to monitor the very ill ones, in fact for patients with eclampsia, the house officers do the vitals… (FGD A02)*

Subtheme 2.2: Fetal/neonatal conditions

Pointers to fetal distress such as meconium-stained liquor, fetal tachycardia or bradycardia, reduced fetal activity and suspected intra-uterine fetal death (IUFD) were associated with increased frequency of vital signs checks and closer patient monitoring. In addition, a response is triggered, which is discussed under the appropriate theme. The following quote from a labour ward midwife with 13 years' experience in maternity illustrates this point:

> *"…From the liquor that was clear before but now turns meconium stained, that should tell you there is fetal distress, or may be when you are getting FHB above 160 or below 120 that is recorded at three different readings within a handful of time of checking, you are sure the fetus is distressed, so you just step up your monitoring frequency, here we connect to the CTG… (KII N02)"*.

If an abnormality is detected in the neonate during the immediate postnatal period, monitoring is continued by the maternity nurses and midwives before a decision is reached on whether or not to refer the baby to paediatricians. The following quotes a nurse KII participant exemplify this observation:

> *"…From the liquor that was clear before but now turns meconium stained, that should tell you there is fetal distress, or may be when you are getting FHB above 160 or below 120 that is recorded at three different readings within a handful of time of checking, you are sure the fetus is distressed, so you just step up your monitoring frequency, here we connect to the CTG… (KII N02)"*.

Subtheme 2.3: Time of presentation

Late presentation is a major problem identified by participants in all three feasibility study sites. The majority of women presenting in labour, especially in Specialist Hospital Bauchi, present in the active phase, with some presenting when the cervix is fully dilated. Also, late presentation to the hospital cut across other categories of patients, including sick pregnant women and those with post-partum complications. The high rate of home births in the communities is believed to contribute to these problems. The following quotes from 2 midwives; a key informant and a focus group participant illustrate this point:

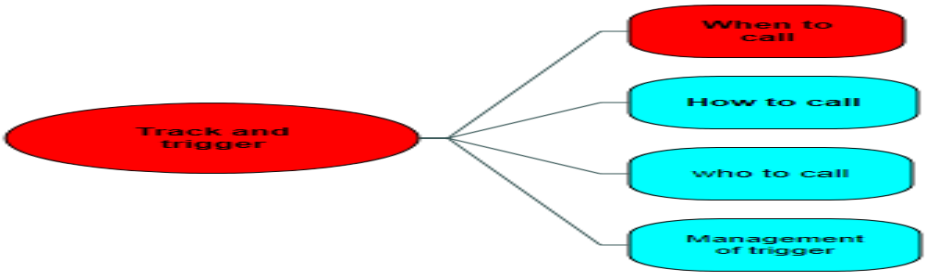
> *"…most of our patients here usually come when the cervix is fully dilated except for few, many of them just stay at home until the labour is active and cervix is fully dilated …(KII B01)"*
>
> *"…You know most of the mothers here believe all normal deliveries should happen at home. They only come to the hospital when all efforts at home have proven abortive… (FGD B05)"*

Many of the late presenters are already "emergency cases" by the time they are seen. As part of the care they receive from the facilities, vital signs are monitored closely, and more frequently than was earlier described (under Subtheme 1.4: Monitoring frequency).

Theme 3: Track and trigger

The callout systems in the three facilities were very similar, except for a few peculiarities in the specialist hospital. This theme was explored under the following related nodes, as illustrated in the visual map below.

Figure 4 8 Themes related to track and trigger



Subtheme 3.1: When to call

There was no guideline regarding when and how a response should be triggered in all three hospitals. This was acknowledged by most interviewees/FGD participants and further substantiated through the non-participant observation across all three study sites. Regarding when to call for help, this was determined at the discretion of the staff undertaking patient clinical monitoring. In general, all circumstances requiring more frequent vital signs monitoring are reported to doctors (discussed previously under Theme 2: Circumstances and how they affect monitoring).

Across all three feasibility study sites, response to what nurses considered a trigger event was similar. Although vital signs were collected and documented routinely (at least once in every 8-hour clinical shift), staff did not consider abnormal vital signs as primary trigger events- clinical diagnoses and frank deterioration in clinical condition of patient are what they considered the situations that warrants escalation of care as illustrated by the following FGD nurse midwives.

"…From vaginal examination for instance, if you have a patient with cord prolapse, or abnormal presentation, you call for help (KII N02)"

"…If the patient is not progressing as expected depending on the parity. You just must call out for help (FGD N02)"

"…If the patient continues to bleed in the postpartum period, is gasping or going into shock, we call the attention of the doctors urgently (FGD A07)"

"… When my patient starts bleeding… (FGD B06)"

"… All patients having eclampsia fits… (KII A03)"

"… Whenever I feel the patient is not making good labour progress… (KII B02)"

Subtheme 3.2: How to call

Seeking help is not always unidirectional (from nurses to doctors), as described earlier under the theme Hierarchy in monitoring. A referral system exists among the nurses and midwives. This happens in all three hospitals (observation). There is always a senior or more experienced midwife in every shift, who is often informed of complicated cases before a response is eventually triggered from doctors. The following quote from a key informant, the matron in charge of the maternity ward in one of the facilities, illustrates this finding:

> *"…well often when you cannot handle issues we have a way of referring still within to some more senior personnel. We make sure there is at least one available in every shift (KII B02)"*

The doctors on call are often within or not far from the labour wards. When help is needed, they are simply asked when they are within the ward. Otherwise, a call is placed using mobile phones, which were available in all wards. Hospital attendants are sometimes sent to call rooms, offices or clinics to call doctors when attempts at reaching them on the phone fail. Occasionally, "call duty" cars are dispatched from the casualty units of the hospitals to pick up doctors on call from home. Contact details of all doctors are made available on the duty rosters. These findings are illustrated by the following quotes of senior KII nurses and were further substantiated through non-participant observation.

> *"…Since we are with them, we normally talk to them directly… KII A03"*
> *"…By phone, we use intercom and call them… KII N01"*
> *"…we send attendants to call them from their offices or clinics… FGD A01"*

Subtheme 3.3: Who to call

An organized referral system exists in the two teaching hospitals with a hierarchy among doctors starting from house officers, through registrars and senior registrars to consultants. At least one house officer (intern) is stationed on the labour ward at all times. For other obstetric wards, all inpatients are assigned to obstetric teams, each of which is assigned an intern that looks after the patients. These house officers discuss all patient-related concerns and their management plans with their

superiors (mainly registrars, but also senior registrars and consultants when necessary). The following quotes of KII doctors illustrates this.

> *"…We have five teams from A to E, each has two HOs and normally they do their rounds every morning. They make some decisions like correcting electrolytes, blood transfusion etc, but are free to discuss any patient with registrars, senior registrars and even us the consultants if necessary… KII A05"*
> *"…Normally my HO takes the consult, clerks and speaks to me when he needs me… KII NO8"*

Although interns are supposed to be the first point of call for nurses, consultations from labour ward midwives often go directly to the registrars. However, triggers for a higher level of care, by senior registrars or consultants, are always decided by the doctors. The following quotes from nurses illustrate these findings:

> *"…we don't call the house officers alone; we call the registrar most of the times. If he cannot manage what is on ground, he normally will call the senior registrar… (FGD N03)"*
> *"…We have a telephone unit here. The telephone unit send the consult to the consultant to come if it's beyond the other doctors on ground… (KII N03)"*

Given that Specialist Hospital Bauchi is not a training institution, there are no registrars, senior registrars or house officers (interns). The maternity complex where all obstetric patients are admitted is managed by a consultant obstetrician and four medical officers (observation). Referral from midwives is sent to medical officers or the consultant on call, as illustrated by the following quotes from the two senior nurse midwives interviewed:

> *"…Normally they call me or any of my three other colleagues during working, or the on call during call hours…then we escalate to our consultant if need be…KII B03"*
> *"…We don't have registrars or senior registrars. Our head of department is an obstetrician and she is very hardworking. Sometimes, we call and discuss patients with her directly when we can't get hold of the medical officers, and she attends to patients even during call hours…. (KII B02)"*

Subtheme 3.4: Management of triggers

While waiting for the doctors to turn up, the midwives offer routine nursing interventions. When they anticipate that a patient might need operative intervention, they prepare her while awaiting the doctor's review. The following quotes from two nurses illustrate our findings regarding the management of triggers by midwives:

> *"…after calling out for help from the doctors, we offer our nursing interventions while awaiting the doctors. For instance, they may come with pyrexia, we attempt to lower the temperature using different techniques such as tepid sponging, administration of analgesics and anti-inflammatory drugs… (KII N06)"*
>
> *"…we call them while you do the immediate monitoring like in a bleeding patient, you estimate the blood loss, (KII N01)"*

Management of triggers among doctors is similar across all study sites. This is dependent on the underlying condition causing deterioration. Broadly, the approach starts from basic principles of patient resuscitation beginning with the primary survey (ABCD). The patient's airway is first secured and oxygen saturation ensured, then breathing, circulation, disability (D-focusing on blood glucose level) are looked into. Often, the concerns are about circulation of bleeding patients manifesting with hemodynamic instability. The house officers (interns) secure IV access, give crystalloids and request grouping and cross-matching of blood simultaneously while assessing the primary cause of bleeding and escalating care to seniors. The management of specific trigger condition varies with the category of obstetric complications underlying each trigger; the following quotes from doctors exemplify how triggers are escalated and managed:

> *"…Two days ago, I was called by the maternity medical officer on call to review an unbooked grand multipara who has sustained cervical laceration following vaginal delivery of a baby with hydrocephalous… he (MO) couldn't identify the laceration and all he told me was that bleeding could not be stopped despite liberal oxytocics… So she was already resuscitated, BP was 100/70 when I arrived... I examined under anaesthesia to identify and repair the extensive cervical laceration…KII B04"*

> *"…It was a case of partial cord prolapse with live baby, the nurses and my house officer had already prepared the patient for emergency caesarean section…we took her to the theatre operated and had a good obstetric outcome…KII N07"*
>
> *"…The head was deeply engaged and I couldn't manipulate it out, so I had to request the senior registrar who was out of the theatre… KII A07"*
>
> *"…Well that is hard to specify, because we are often called in to review patients by nurses and junior colleagues for varying reasons…KII N08"*

Theme 4: Staff attitudes

Attitudes of nursing staff to patient monitoring and caregiving were explored in the FGDs, and more importantly the KIIs, as most of the KII participants were line managers. Findings from most FGD participants revealed that staff attitudes to monitoring and caregiving are generally good. A few acknowledged some lapses, rationalizing it in terms of staff capacity and other challenges. The following quotes of senior nurses illustrate these findings:

> *"… Everybody is trying his best to ensure patients feel at home, everybody that come here regardless of his tribe or religion is treated with utmost respect… (FGD N03)"*
>
> *"…It is mixed really, we have the good ones and the bad ones, you cannot generalize, but I think man power challenges contribute a lot to staff attitude here… (FGD B03)"*
>
> *"…I will say that the attitude is fair, I will not give us 100% we have lapses in the sense that we don't have enough staff (FGD A01)"*

Overall, staff attitudes to monitoring were better among the workers (nurses and midwives) in the two teaching hospitals compared to those in the specialist hospital. The staff in charge of the maternity wards of the three hospitals were among the KII participants. Both labour ward line managers in the teaching hospitals reported being happy with their staff's attitudes as illustrated by the following quotes:

> *"…I don't need to tell you, you see it yourself, I wish you had met Nurse "X" (*she called a name*) she is my best nurse here, I don't just take anybody, I have the best here… (KII A05)"*
>
> *"…It's very good to be honest, because to work in the labour ward you must have passion for the job… (KII N03)"*

The head of the maternity complex, where all obstetric patients in the non-teaching hospital were managed, reported being very unhappy with her staff's attitudes to patient monitoring and care. The following quotes from her illustrates this finding:

> *"… no, things are just going downhill unlike before, that is just the fact. I don't know whether it is because the interest is no more there, but ideally, a staff is not supposed to wait to be told do this do that, you know what you suppose to do, but these days, I just don't really know what to say…KII (B02)"*

Research question: What is the perception of health workers of EWS and its acceptability?

Themes 1 and 2: Perception and acceptability

The above research question was explored under two separate themes, perception and acceptability. Although many challenges were identified by participants as potentially constituting a bottleneck to MEOWS implementation, most participants had a positive perception of the innovation. The challenges are discussed under the appropriate themes. A summary table of the NVivo 11 analysis output of these themes with evidence from selected quotes is provided as an appendix (**Annex 4F5**).

The majority of participants expressed readiness to accept and optimism on the overall acceptability of the systems if implemented in their workplaces. The following statements from nurses and doctors illustrate these findings:

> *"…come to think of it if an obstruction is detected early, a caesarean section is immediately done, right. Hypertension is detected early and addressed, malaria is dealt with early, so what are we talking about… (KII A05)"*

> *"…the idea is very much welcome and since we are looking forward to developing our medical practice to what is obtainable in the developed world, this is going to be a major step (FGD B06)"*
>
> *" …it is a good idea that you are working on this tool, because maternal and infant mortality have become a burden to us and we really want to reduce them… (KII B03)"*
>
> *"…the system will be quite useful as it will alert us on when to call for help regarding a patient, and this will enhance early and timely intervention. So, will be very beneficial to both staff and patients. So, it's going to be very useful to us… (KII A03)"*
>
> *"…the idea is very much welcome, because in most instances, vital signs are indicators to maternal problems, so if vital signs are recorded as they should, and this tool is put into good use, I can see good prospect in the struggle to reduce maternal morbidity and mortality… KII N08)"*

Research question: What potential challenges could affect EWS implementation and what are the possible solutions?

The above research question was explored under two key themes, the challenges anticipated and possible solutions. A summary table of the NVivo 11 analysis output of these themes with evidence from selected quotes is provided as an annex (**Annex 4F6**).

Theme 1: Challenges

Subtheme 1.1: Human resource challenge

Regarding the first theme (Challenges), the human resource for health was a major challenge in all the three feasibility study sites and more so in Specialist Hospital Bauchi. Both the KII and FGD participants identified this challenge and it was further substantiated in the non-participant observation; the average nurse-to-patient ratio in the observed wards was 1:7 in Specialist Hospital Bauchi, and 1:5 in the two teaching hospitals (observation). The following quotes 2 nurse KII participants illustrate the above finding:

> *"…Ideally, a midwife should nurse one patient. In a situation where you have one to six, one to eight what do you expect? Sometimes we have fifteen patients here in the labour ward and you will find only two nurses in a shift… (FGD A02)"*
> *"…we don't have enough staff, like in labour ward here you might have 2 or 3 nurses on duty one is in the theatre where C/S is going on, so you are now left with 2 or 1 monitoring 10 patients in labour… (KII A01)"*

Considering the above challenge, the high workload was a major concern raised by participants that could possibly affect EWS implementation. As part of the activities undertaken during the observation, record-keeping was checked among staff and previous records were cross-examined for comparison and triangulation. Partographs were not used to monitor labour in Specialist Hospital Bauchi. This was attributed to high workload, as illustrated in the following quotes from two KII participants:

> *"…you know ideally, if a woman comes into labour ward, after you examine her, in those days when we have the partograph you will have to put her on partograph …(B02)"*
> *"…challenges often result from inadequacy of man power. It is not that you don't want to do the work but whereby the problem is just too much work on you, you just try to see what you can do and leave the rest… (B01)"*

However, midwives in labour wards of the two teaching hospitals started partographs for all patients admitted during our observation period, and the charts were used to monitor all women giving birth during this period. Cross-examination of partographs completed in the week preceding the period of observation revealed similar findings. The nurses and midwives in all three hospitals kept updated vital signs charts that consisted of temperature, pulse, respiratory rate, blood pressure and fetal heart rates recorded at least once in every shift (three times in 24 hours). This chart was also cross-examined for the week preceding our observation, and findings in the three hospitals consistently agreed with what was observed.

Subtheme 1.2: Equipment challenge

Another challenge was insufficient patient monitoring equipment. This challenge was also more pronounced in Specialist Hospital Bauchi. An inventory of functioning monitoring equipment was taken during the direct observation and the findings are presented below (**Table 4.7**).

Table 4 7 Inventory of functioning monitoring equipment in the labour wards of the feasibility study sites

Equipment	Bauchi	Abuja	Zaria
Digital BP Machine	0	1	1
Manual BP Machine	1	2	2
Stethoscope	1	3	2
Thermometer	1	2	2
Foetal stethoscope	1	2	1
Cardiotocograph	0	3	1
USS (in labour ward)	0	1	1
SPO2 Machine	0	2	1
Digital monitor	0	1	1
Glucometer	0	2	1
Urinalysis strip	None	Available	Available
Side laboratory	None	Available	Available

The limited number of monitoring equipment, plus other logistic concerns, such as insufficient stationery and medical consumables, were identified by participants as other challenges to effective patient monitoring and care. The following quotes from junior nurse midwives illustrate these findings:

"…like here for instance, we have only one BP machine on the ward so can you imagine? It is not enough. In fact, when our doctors are in ward rounds, they often take our only BP apparatus, so we keep rotating the machine between them and ourselves… (FGD B03)"

"… to take the pulse and respiratory rate you only need your wrist watch, so that one is not a problem, but for temperature and blood pressure, if there is no apparatus to take them, there is nothing you can do about it… (FGD B06)"

Subtheme 1.3: Other challenges

Accepting an innovation is often associated with resistance, as some participants have pointed out. Some resistance may, therefore, result among staff following the implementation of EWS. However, with time, especially when the usefulness of these systems in the hospitals becomes more apparent, staff will eventually accept and use the charts for monitoring. The following quote from a senior nurse and a consultant obstetrician illustrates this finding:

> *"…you know it takes time for people to accept a new thing, some will be bored doing it especially at the early stage, but as time goes on and it becomes part of them, they will eventually accept it as the routine… (KII N01)"*
> *"…Doc you know Rome was not built in one day…surely, there will be a lot of resistance, especially from our nurses downstairs (meaning in the labour wards). Once they believe in something, it's really hard to change them, but am sure we will get there soon…KII A06"*

Theme 2: Measures

Measures to ensure the feasibility of use of these systems should be centred on addressing the specific challenges in the hospitals. Human resource challenges and equipment shortages should be addressed by the governments and managements of the hospitals. These are, however, not specific to early warning systems. Training and retraining of staff on how the chart is used is a potentially useful measure suggested by most participants. This should include incorporating EWS into the teaching curriculum of nurses and midwives during their training. Also, in order not to increase paperwork in facilities that still use partographs in their labour wards, some participants suggested incorporating early warning scores into the partographs for easier and more holistic patient monitoring. Including EWS charts in nurses' handover documents and ensuring the charts are adequately completed before patients are taken over are other potentially useful measures to ensure successful implementation. The following quotes from nurses and midwives illustrate these findings:

"…there should be adequate man-power, also, we need more equipment; we need electronic monitoring machines. I really don't see us achieving much without these gadgets… (FGD N05)"

"…I will recommend training and retraining of healthcare personnel, particularly we, the nurses and including this into curriculum of our training institutions, so everyone learns how to use the tool … (FGD A03)"

"…I think it is worthwhile thinking, including the charts in our handover documents. For instance, the staff on afternoon shift would ensure that all inpatients have correctly completed charts before agreeing to take over from morning staff. This will go a long way ensuring strict adherence…KII B02"

On their part, the doctors suggested making presentations on EWS at clinical meetings and grand rounds. Approval should be sought at management level to substitute the routine vital signs charts with EWS charts as the latter achieve both purposes. On the wards, doctors could insist on having patients' EWS scores before making clinical decisions during ward rounds as this would potentially persuade the staff responsible to be adherent. Additionally, frequent surveillance by matrons in charge of all relevant obstetric wards and imposition of sanctions on responsible staff that are found wanting are other potentially useful measures. The following quotes from doctors support the above findings:

"… The most important measure in my opinion is strong support from the hospital management. If you get them to approve this instead of our TPR chart, it will become a law! After all, they look similar and the chart has all the information on our TPR. Anybody who fails to comply would be sanctioned…KII A07"

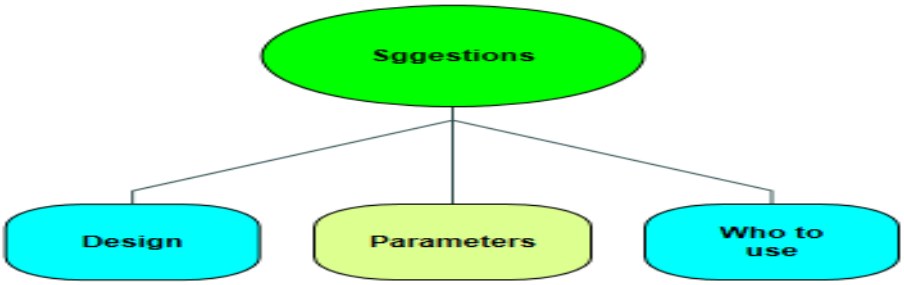
"…On our part (doctors) we can have a presentation in our departmental academic team meeting on the chart, and this should be continuous because every three months, we have new interns coming in who actually monitors our very sick patients, and need to know how the chart works…KII N09"

> *"…The matron in charge of our maternity complex here is a very experienced midwife and a good administrator, she is being highly revered by the maternity staff, so getting her to institute an active surveillance system will be very helpful…KII B04"*

Research question: What are the suggestions regarding EWS design and implementation?

A sample of the MEOWS chart used in the Liverpool Women's Hospital was given to participants and the principles on which the chart works, including clinical scenarios, were discussed during interview sessions. Suggestions were obtained from participants on our chart's design. This was explored under the related themes in the ensuing subsections (**Figure 4.9**). A summary table of the NVivo 11 analysis output of the related themes with evidence from selected quotes is provided as an Annex (**Annex 4F7**).

Figure 4 9 Themes related to suggestions on early warning charts



Theme 1: Design

The majority of the participants opined that paper-based systems are more likely to work at present. This is because all patient care and monitoring activities in the three hospitals are documented on paper. Moreover, most of the nursing staff are not computer literate and would require intensive training to use any computer software. The following quotes KII nurses illustrate these findings:

> *"…if it is in the computer, it is only when you are computer literate that you can use it. It will be more helpful in a paper form at least for now… (KII B02)"*
> *"…for now, that computer is not routinely used in this hospital, I think we should introduce a paper, but as time goes on, it should be computerized, so we can easily switch to the soft version in the computer… (KII A02)"*
> *"…We will have loved to go electronic like what is obtainable on the other side, but you see doc, this is the fifth year since electronic record was approved in this hospital, most clinical staff were trained and computers were secured, but we are still yet to switch due to unknown factors. So for starters, the paper-based system is more likely to succeed…KII N06"*

In choosing between score-based (black-and-white) and colour-coded charts, all clinicians interviewed suggested a colour-coded EWS chart similar to what is obtainable in the UK (MEOWS) and other well-resourced settings. This according to them is less labour-intensive and more visually appealing.

An early warning chart as an Android app was also suggested by some focus group participants to ease their work of patient monitoring and make it less boring. In their opinion, this is necessary as their hospitals need to move with the times and the technological advancement of the new world. The following quote from a nurse FGD participant with five years' work experience in maternity illustrates this finding.

> *"…my own view is we are in a new world, and virtually all the health workers have android phones, so if it's on the phone as an android app, it will be easier and more interesting to work with. It will even lessen our paper work, and you know, you don't need to stress your brain, the app will calculate the score for you. Even if one person doesn't have an android phone, some other persons in the team could have so both can use the app together… (FGD N02)"*

Theme 2: EWS parameters

Vital signs including temperature, pulse rate, respiratory rate and blood pressure are monitored routinely in all hospitals despite the challenges identified. Monitoring of urine output, PV bleeding and amniotic fluid colour, assessment of consciousness level, and scoring of pain severity were also suggested for inclusion as observing these parameters does not require any equipment. Although suggested for inclusion in the chart by participants from the two teaching hospitals, oxygen saturation (SPO2) monitoring is not routinely performed in Specialist Hospital Bauchi, as the equipment is not available. The following quotes of 3 nurses (KII N01, N02, FGD N02) and a doctor (KII B03) elucidates the above findings:

> *"…the basic temperature, pulse, respiration, BP and oxygen concentration are things we routinely monitor in all our patients here…. (KII N02)"*
>
> *"…Oxygen saturation too should be included in the chart, because it is readily available here… (FGD N02)"*
>
> *"…for sick pregnant women, or those postpartum you still monitor for bleeding, colour of liquor or lochia and consciousness level. All these do not require equipment and are quite helpful, so I think should also be included as in the sample chart… (KII N01)"*
>
> *"…In addition to the routinely monitored vital signs, lactate level is an important indicator of sepsis, but not even an ABG machine, we do not have a functional pulse oximeter in the whole of the maternity complex...KII B03"*

For women in labour, some participants in the two teaching hospitals suggested that an early warning system should be incorporated into the existing partograph for ease of use. This is because the basic vital signs are already recorded in the partograph, so it is only necessary for them to be scored and risk appropriately assessed. The following quote from a nurse KII participant illustrates this:

> *"…for us in the labour ward, I think the monitoring chart will be much more useful if there is a way it can be incorporated into the partograph, so that monitoring can be done for each patient as a whole … (KII N02)"*

Theme 3: Who to use the EWS

The early warning chart should be used primarily by nurses and midwives undertaking maternal monitoring in related hospital wards. Doctors (especially the house officers) occasionally take part in patient monitoring and would also find EWS useful. The following quotes from 2 senior nurses illustrate this finding:

> *"…the midwives and the doctors too especially the junior ones… (KII A01)"*
>
> *"…I will suggest that it gets to the primary health care centres because most of the patients end up there. This will help those facilities recognize complications early and in determining when to refer… (KII N02)"*

4.7. Putting key differences in context of study sites

The three feasibility study sites were all tertiary healthcare facilities located in urban areas across three geopolitical zones of northern Nigeria. Rationale for selection of these facilities has been discussed previously (Chapter 3: Methodology). While one is a relatively understaffed non-teaching (specialist hospital) situated in Bauchi state, in the North-east geopolitical zone, the other two (National Hospital Abuja, and Ahmadu Bello University Teaching Hospital Zaria) are both teaching hospitals located in the North-central and North-east geopolitical zones, respectively.

The three hospitals together admitted 5802 women for childbirth or complications of pregnancy over the twelve-month study period; these included 2362 admitted to maternity complex of specialist hospital Bauchi, 1510 and 1930 patients admitted to labour wards, lying-in wards obstetric wards and intensive care units of National Hospital Abuja and ABU teaching hospital Zaria respectively. Estimated MMR was highest in Bauchi, at 1376.4 per 100,000 live births. Abuja and Zaria had MMR of 1075 and 1138.4 per 100,000 live births, respectively.

Unlike in the teaching hospitals, there are no registrars, senior registrars or house officers (medical interns) in specialist hospital Bauchi. The maternity complex where all obstetric patients are admitted is managed by a consultant obstetrician and four medical officers. Referral from midwives are sent directly to medical officers or the consultant. Estimated clinical staff (nurses/midwives and doctors) to

patient ratio was approximately 1 to 7 in specialist hospital Bauchi, and 1 to 5 in National Hospital Abuja and ABU teaching hospital Zaria. This is consistent with a recent report that similar referral hospitals in Nigeria are overloaded beyond their human resource for health capabilities (Koce et al, 2019), which explains the disparities in maternal deaths and direct obstetric complications rates (Table 4.4).

Consequent upon human resource for health shortage, healthcare providers in such facilities become over-burdened with largely minor ailments that could have been easily addressed at lower level healthcare facilities (Makama et al, 2015; Koce et al, 2019). The role of these hospitals as referral facilities in managing advanced medical conditions and engaging in research is noted to be seriously undermined in the Nigerian healthcare system (Abodunrin, 2010). This may explain our findings of poor attitude of nurses and midwives to clinical monitoring, and resultant failure to use partograph for monitoring women in labour in maternity units of specialist hospital Bauchi, but not in the two teaching hospitals.

Although insufficient monitoring equipment, stationery and medical consumables, was a challenge across all three feasibility study sites, this was also more pronounced in specialist hospital Bauchi, as illustrated by Table 4.7.

Overall however, findings related to the two feasibility study's objectives- patient monitoring practices including existing trigger mechanisms, and perception of EWS- were essentially similar across the three hospitals as summarised in subsection 4.8 below.

4.8. Chapter summary

Chapter 4: Feasibility study

- The chapter presented a phase of this PhD research project conducted to assess the feasibility of implementing obstetric EWS in three Nigerian tertiary hospitals.
- The study was predominantly conducted in northern Nigeria. Facilities were purposively selected to be representative of the three geopolitical zones of this region.
- Mixed data collection methods were used, consisting of quantitative review of secondary records, qualitative interviews (20 KIIs with doctors and senior nurses/midwives), focus groups (three FGDs with junior nurses and midwives) and direct non-participant observation.
- Among the 5802 annual obstetric admissions, 22.6% had obstetric haemorrhage, hypertensive disorders, sepsis, or prolonged/obstructed labour.
- Estimated LBR was 95.1%, of which 71.3% were spontaneous vaginal, 3.5% instrumental vaginal and 25.2% caesarean births (16.1% emergency and 9.1% elective C/S).
- SBR was 48.7 per 1000 live births, estimated MMR was 1218.1 per 100,000 live births, and ICU obstetric admission rate was 2.8%.

- Maternal monitoring was primarily performed by nurses and midwives, with their roles varying with staff experience. Junior doctors (interns) undertook vital signs monitoring of severely complicated cases (e.g., patients with eclampsia).
- Pulse, respiratory rate, BP and fetal heartbeat are recorded at least once in every labour ward shift, and stable obstetric inpatients have these parameters monitored 12-hourly. Deteriorating maternal or fetal clinical condition necessitates more frequent monitoring.
- Escalation of care happens within and between nurses/midwives and doctors through verbal messages, hospital assistants, phone calls or dispatching of call vehicles; no bleep system exists in any facility.
- What constitutes a trigger is determined at the discretion of clinical staff; no protocol/guidelines exist on how clinical conditions affect maternal monitoring, or how triggers should be escalated and managed.
- Trigger conditions are perceived by most participants as clinical diagnosis rather than abnormal findings of vital signs.
- Referrals from midwives are often sent to registrars directly, and further escalation is performed by doctors.
- Human resource and equipment shortages are potential challenges to EWS implementation; staff/patient ratio is 1:7 in Bauchi and 1:5 in the two teaching hospitals.
- Most participants were positive about EWS and expressed readiness to accept the innovation.
- Suggestions were offered to ensure successful implementation. On a broader note, these include addressing human resource and equipment challenges by relevant authorities, incorporating EWS teaching into the nursing and midwifery curriculum and getting management approval to use EWS in place of routine vital signs charts. Other measures include use of paper-based charts for a start, incorporating EWS in partographs, instituting surveillance and audit systems, ensuring EWS are complete at nurses' handover, and repeated presentations at doctors' meetings for incoming interns and new staff.

4.9. Conclusion

This study confirms the absence of an early warning chart, a checklist or any guidelines on how to trigger response to or manage obstetric emergencies in all three health facilities studied. Maternal monitoring practices and scope of work of nurses and midwives were hampered by challenges including increased workload related to inadequate human resource for health and insufficient or inefficient equipment required for patient monitoring. Despite these challenges, the most constantly monitored parameters in obstetric EWS (vital signs) (Umar, A., et al*.*, 2019), including the most sensitive variable (respiratory rate), are monitored in all three hospitals. However, the understanding of the potential use of these parameters as early warning pointers to maternal deterioration is deficient among participants. This, therefore, implies that implementing EWS will enable healthcare staff to make meaningful use of routinely monitored clinical parameters without significantly impacting on their workloads. Also, the study found that most participants were positive about obstetric early warning charts and are prepared to accept and use the chart for maternal monitoring if it is introduced in their facilities.

Chapter 5: Design and validation of EWS model

5.1. Overview of the chapter

This chapter presents the second phase of the study: the development and validation of a simple obstetric diagnostic prediction model and EWS for use in resource-limited settings. The chapter starts by providing a brief rationale for this analysis, followed by a description of the study design, source of SMO cases data set and control data collection. Next, the ethical consideration guiding use of the secondary data, model design, internal validation process, conversion of the model to score-based monitoring chart, and sensitivity analysis/quality assurance measures taken are described. Finally, the overall analysis and resulting EWS model is discussed in the context of literature on EWS validation and effectiveness studies. The chapter ends with conclusions and summary of key points.

5.2. Rationale

The UK's Confidential Enquiry into Maternal and Child Health (CEMACH) (2003-2005 report) recommended "the use of obstetric EWS to improve timely recognition, treatment and referral of women who have or are developing a critical illness" (CEMACH, 2007). Although widely adopted by maternity units both within and outside the UK, most of the available obstetric EWS versions used subsequently were designed based on clinical consensus rather than the application of recommended prediction model development methodology that should include statistical analysis of outcome measures (Isaacs et al., 2014; Austin et al., 2014; Edwards et al., 2015; Hedriana et al., 2016; Mhyre et al., 2014; Ryan et al., 2017; Shields, 2016; Singh et al, 2012).

Model development involves statistical combination of predictor clinical observations into a multivariable Clinical Prediction Rule (CPR). The Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement recommends that new prediction models are tested on data used in its development (internal validation) and other data not used in its development (external validation) (Collins et al., 2015a).

In 2013, the first statistically derived, clinically modified obstetric EWS was developed and internally validated using clinical observations (physiological variables) collected from 4400 women during their first 24 hours of critical care admission (Carle et al., 2013a). The resulting clinical EWS developed showed a good predictive ability to discriminate survivors from non-survivors in the derivation data set, and on an external data set (Paternina-Caicedo et al., 2017). However, since the database used in the development, internal (Carle et al., 2013a) and external validation (Paternina-Caicedo et al., 2017) of the EWS were only for women admitted to critical care, the EWS may not be suitable for obstetric population without obvious need for critical care and from other settings.

Additionally, no obstetric EWS has been developed and/or validated using data primarily collected from a low-resource setting. Giving that most obstetric EWS identified in a recent systematic review (Umar, A., et al., 2019) had simple clinical variables that are readily collected in low-resource settings despite existing challenges (**Chapter 4**: Feasibility study) (Moore, Thomson, Pimentil, Fekad, & Graham, 2019), it was deemed necessary to design an obstetric EWS for use such settings with a view to improve the quality of care and reduce the overwhelming burden of maternal morbidity and mortality in these settings.

5.3. Objectives

The objectives of phase were as follows

- To construct and internally validate an obstetric early warning clinical predictive model for severe maternal outcome using data from obstetric ward admissions in to tertiary healthcare centres in low-resource settings.
- To generate from this model, a simple score-based patient monitoring chart for use in low-resource settings.

5.4. Methods

5.4.1. Study design

A quantitative retrospective (case-control) analysis of secondary data was used to achieve the study objectives. Records of women admitted to inpatient obstetric wards in Nigerian tertiary hospitals were used for the analysis. Cases based on standardized definitions were derived from the Nigerian near-miss study, the largest prospective investigation of maternal deaths and near misses in Africa

(Oladapo et al., 2016). Controls were women who were admitted for obstetric care at the same time as the cases. These admissions took place between June 2012 and August 2013.

5.4.2. Study population and data sources

The study protocol and findings of the Nigerian Near-miss study have been published elsewhere (Oladapo et al., 2016; Oladapo et al., 2009). In brief, the design was a nationwide cross-sectional study. All (46) public tertiary hospitals providing obstetric services (university teaching hospitals and Federal Medical Centres) within the six geopolitical zones of Nigeria were targeted for inclusion into the survey. Of these, 42 hospitals provided consent, participated and successfully implemented the study (Oladapo et al., 2016).

All women admitted to the participating hospitals for birth or within 42 days of birth/termination of pregnancy between June 2012 and August 2013 were eligible for enrolment into the near-miss study. The study reported severe maternal outcome (SMO) cases based on the WHO near-miss criteria (organ dysfunction, clinical and management-based) (Oladapo et al., 2016; Say et al., 2009).

We included data from all 4360 women who had SMO during the 14-month surveillance. Of these women, 998 died and 3362 suffered maternal near miss as defined by Say and colleagues (Say et al., 2009). One thousand women who were admitted to three of the 42 hospitals for birth and discharged without any SMO were the controls. Control data were collected from secondary records by the principal researcher and research assistants across the three hospitals. All data were collected within 24 hours of occurrence of SMO (for cases) or 24 hours of birth/end of pregnancy (collected retrospectively for controls).

5.4.3. Data abstraction

Individual-level data on all study variables were abstracted from the near-miss study data set (n=4360) and from the case notes of 1000 controls. These included demographic characteristics (age, weight, height), obstetric variables (parity, number of antenatal clinic visits, gestational age at time of admission/delivery, delivery mode, interval from last pregnancy, number of previous caesarean section), diagnosis, length of stay in hospital, and the last haematocrit measured. Abnormal clinical indices were abstracted from the cases data set based on their

definitions codebook including high (>140 mm Hg) and low (<90 mm Hg) systolic blood pressure, high (>90 mm Hg) and low (<60 mm Hg) diastolic blood pressure, high (>38°C) and low (<35°C) temperature, marked tachycardia (PR>120/min) and bradycardia (PR<60/min), hypoxaemia (SpO_2<90%), severe tachypnoea (RR>40/min) and bradypnea (RR<6/min), severe oliguria (urine output<300 mL in 24 hours), and coma (Glasgow Coma Score<8/15). Among the controls, the data were collected as continuous variables and classified based on the cut-off values in the cases data set codebook.

5.4.4. Outcome

The outcome measure for this analysis was SMO, computed as the sum of maternal deaths and near misses and transformed into a binary variable - occurred or not. Maternal death was defined according to the International Classification of Diseases (ICD-10) (definition of terms in **Chapter 3**: Methodology). Women were identified as a maternal near miss if they met any of the three near-miss criteria (clinical criteria related to specific disease entity, intervention-based criteria and organ system dysfunction-based criteria)(Say et al., 2009).

5.4.5. Statistical methods

The characteristics of the study population were summarized by means and standard deviations for continuous variables and percentages for categorical variables. Continuous variables were compared between cases and controls through analysis of variance or Kruskal-Wallis tests, depending on whether variables were normally distributed or not. Normality was assessed visually through distribution plots and with the Shapiro-Wilk test. Data for 1200 study participants were randomly sampled from the combined data set and randomly allocated into the development data set (n =600) or validation data set (n=600) with two controls per case. This sample size estimate was based on a baseline SMO prevalence of 4.8% (Oladapo et al., 2016). At 5% level of significance, the analysis could detect an absolute difference in SMO prevalence of 6% and 5% at 90% and 80% powers, respectively.

5.4.6. Model building

Univariable logistic regression models were fitted to assess the association between each predictor variable and outcome (SMO), in turns. A stricter inclusion criterion was applied and therefore variables were only selected from the univariable models

for inclusion into the multivariable model if the model p-value was <0.05. This yielded 22 potential factors for inclusion.

Multivariable logistic regression models were fitted using the backward stepwise approach and factors were removed from the model one at a time based on the highest p-value>0.05 and their likelihood ratio. When the final model was achieved, a sensitivity test was performed by including each of the eliminated variable, in turn, into the final model to assess their significance. None of these were found significant in the final model. One variable (diastolic blood pressure) was dropped from the model for collinearity with other variables. We verified the collinearity by a simple check of the correlation between the suggested variables.

5.4.7. Model performance

Performance of the obstetric EWS clinical prediction model from the derivation data set was tested on the two validation data sets (Altman & Royston, 2000). First, the overall validity (sensitivity, specificity, negative predictive value-NPV and positive predictive value-PPV) as well as the area under curve (AUC) for the ROC curves were assessed for the final model. Discrimination was assessed using the *c* statistic or AUC, an estimate of the probability of assigning a higher risk to those who suffered an SMO compared to those who did not. The final model was then applied to the validation data set and the performance was similarly assessed. Finally, we estimated validity of the selected EWS predictors by applying the final model to the entire (n=5243 after excluding missing data) data set of cases and control, bearing in mind that the ratio of cases to controls had been reversed – more than four cases per control. All statistical analyses were performed using the SPSS version 25 and Stata version 15.1. We constructed 95% confidence intervals (95% CI) for all performance characteristics.

5.4.8. Obstetric EWS score-based monitoring chart

Our statistically derived diagnostic prediction model was modified based on clinical importance of rejected variables. Given that the cases data set provided categorized (binary) clinical variables, it was not feasible to validate reference ranges for the different model parameters. Hence, the final modified obstetric early warning system model was converted into simple score-based monitoring chart

using the reference range proposed in the MEOWS chart recommended in the 2007 CEMACH report (**Chapter 1: Appendix 1A**).

5.5. Ethical considerations

Clearance was obtained from the principal investigators of the Nigerian Near-miss study (through WHO, Geneva, Switzerland) for the use of the data. A data use agreement was signed in which the PIs indicated that this analysis was covered under the approved use of data by the Ethics Review Committees both at the WHO and all 42 participating hospitals. However, additional approval for this study was obtained from the Research Ethics Committee of the Liverpool School of Tropical Medicine (Protocol ID 17-047).

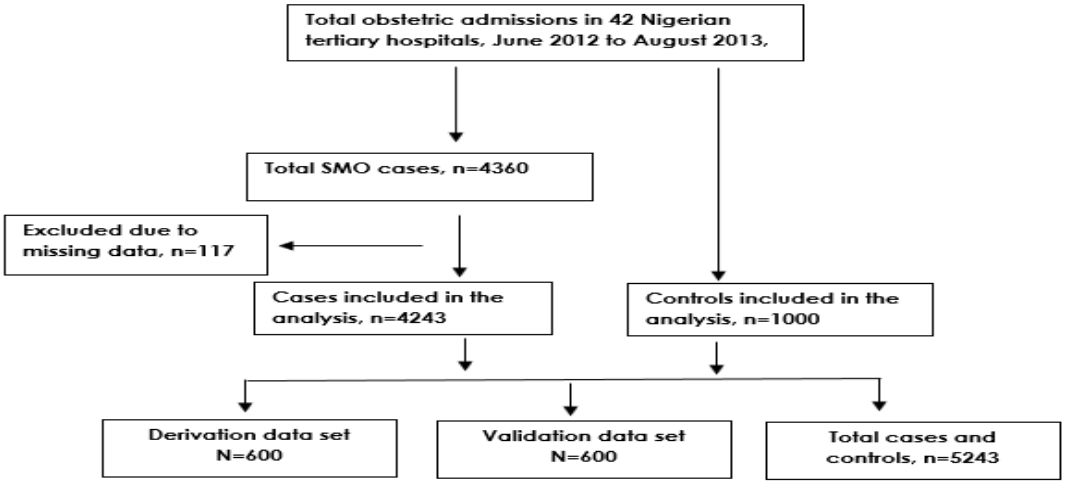
We present our findings according to the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis statement (Collins et al., 2015a).

5.6. Results

5.6.1. Background characteristics

From the 100,107 women admitted for pregnancy, childbirth or puerperal complications during the 14 month period of the Nigerian Near-miss study, 4360 developed SMO and their data were included in the cases data set. Of these, 998 women died and 3362 suffered maternal near miss. A total of 117 (2.7%) women with SMO had missing data, with no records of type of SMO (death or near miss) they experienced. Data from these women were excluded from the analyses, as the missingness was assumed to be completely at random. The lack of data on other characteristics of these participants did not allow for assessment of bias in dropping them from the analysis. None of the control participants had missing parameters. **Figure 5.1** illustrates allocation into, and composition of, the development and validation data sets.

Figure 5 1 Creation of the development and validation data sets



Characteristics of the SMO cases and the controls are given on **Table 5.1**. Those who experienced SMO tended to be older and more likely to be obese. They also stayed longer in hospital, with mean number of days on admission four times greater than the controls and were more likely to be anaemic. There was no significant difference in terms of parity, but SMO cases tended to have more preterm births and had significantly shorter duration from last pregnancy.

Table 5 1 Characteristics of severe maternal outcome cases (n=4243) compared with controls who were discharged after normal vaginal birth (n=1000)

Variable	SMO cases	Controls	P-Value
Age at baseline, mean (SD)	27.8 (6.5)	26.8 (6.1)	<0.001
Weight on admission, mean (SD)	75.7 (14.9)	67.2 (13.9)	0.002
Height in meters, mean (SD)	1.6 (0.1)	1.6 (0.3)	0.125
Days on admission, mean (SD)	6.8 (5.2)	1.6 (0.7)	0.040
Number of ANC Visits, mean (SD)	4.6 (3.5)	3.6 (2.9)	<0.001
Last PCV, mean (SD)	27.6 (9.8)	33.3 (5.9)	<0.001
Parity, mean (SD)	4.5 (2.0)	4.4 (1.0)	>0.050
Gestational age in weeks, mean (SD)	35.8 (4.5)	38.4 (4.7)	<0.001
Months since last birth, mean (SD)	3.3 (1.9)	4.8 (1.9)	<0.001

5.6.2. Model creation

Overall, women who had abnormal clinical observation measurements (either lower or higher than normal), based on the predefined cut-off points deciphered from the cases data set, were more likely to develop SMO than the controls (**Table 5.2**). Initially, univariate analyses were performed considering all 22 potential variables for entry in the model and SMO outcome variable. Of these, a total of 15

had a significant p-value (<0.05) (**Table 5.2**), and so these were considered for potential inclusion in multiple regression model.

Table 5. 2 Statistically significant clinical variable from univariate analysis (dependent variable; SMO binary outcome variable)

Parameters	Cases N=200	Controls N=400	Chi-square significance
High systolic blood pressure (>140mHhg), *number (%)*	75 (68.8)	34 (31.2)	<0.001
Low systolic blood pressure (<90 mHhg), *number (%)*	58 (61.7)	36 (38.3)	<0.001
High diastolic blood pressure (>90 mHhg), *number (%)*	75 (64.7)	41 (35.3)	<0.001
Low diastolic blood pressure (<60 mHhg), *number (%)*	110(65.5)	58 (34.5)	<0.001
Severe tachypnoea (RR>40/min), *number (%)*	26 (92.9)	2 (7.1)	<0.001
Severe bradypnea (RR<6/min), *number (%)*	5 (100)	0 (0)	<0.001
Fever (Temp>38/min), *number (%)*	17 (94.4)	1 (5.6)	<0.001
Marked tachycardia (PR>120/min), *number (%)*	58 (71.6)	23 (28.4)	<0.001
Hypoxaemia (SP02<90%), *number (%)*	14 (82.4)	3 (17.6)	<0.001
Caesarean section in present admission, *number (%)*	51 (94.4)	3 (5.6)	0.001
Low urine output (300ml/24hours), *number (%)*	12 (100)	0 (0)	<0.001
Prolonged unconsciousness (GCS<8/15), *number (%)*	14 (100)	0 (0)	<0.001
Blood transfusion in present admission, *number (%)*	40 (67.8)	19 (32.8)	0.038
Last haematocrit level, *mean (SD)*	27.6 (9.8)	33.3 (5.9)	<0.001
Days admitted, *mean (SD)*	6.8 (5.2)	1.6 (0.7)	0.040

The significant variables were entered into a multiple logistic regression model. Both backward and forward stepwise selection methods were used to build the final parsimonious model, with the standard 5% significance level for entry and removal. Both techniques produced the same final model, in five steps, with eight parameters (high systolic blood pressure (>140 mm Hg), low systolic blood pressure (<90 mm Hg), high diastolic blood pressure (>90 mm Hg), severe tachypnoea (RR>40/min), fever (temperature >38^{o} C), marked tachycardia (PR>120/min), delivery mode (caesarean or vaginal birth), and number of previous caesarean births).

5.6.3. Risk of severe maternal outcome

Table 5.3 gives the odds ratios of developing SMO for the variables in the final model. The risk of developing SMO was five times greater among women with high systolic blood pressure (>140 mm Hg) and tachycardia (PR>120/min), while low systolic BP (<90 mm Hg) increased SMO risk by four times. Caesarean delivery

during index admission was found to increase risk of SMO significantly (absolute risk of six), but number of previous caesarean sections according to the model did not increase risk. Most importantly, the variables with the highest risk of SMO in the model were fever and tachypnoea, with absolute risks of 117 and 25 respectively.

Table 5 3 Results of multiple logistic regression analysis using significant predictor variables (n=15) from univariate analysis: Outcome variable is SMO

Development Model (n=600)						
Parameters	**Odd ratio**	**S. E**	**Significance (p)**	**95% CI**		**Absolute risk***
				Lower	**Upper**	
sBP>140	5.26	0.49	0.001	2.03	13.63	5
sBP<90	3.73	0.42	0.002	1.65	8.41	4
dBP>90	2.78	0.48	0.035	1.08	7.16	3
RR>40	25.20	0.92	<0.001	4.19	51.60	25
Temp>38	116.51	1.12	<0.001	12.96	147.42	117
PR>120	4.62	0.43	<0.001	2.00	10.66	5
CS (Yes vs No)	5.91	0.38	<0.001	2.79	12.53	6
Number of CS	0.96	0.01	<0.001	0.95	0.97	1
Validation model (n=600)						
Parameters	**Odd ratio**	**S. E**	**Significance (p)**	**95% CI**		**Absolute risk***
				Lower	**Upper**	
sBP >140	10.01	0.67	<0.001	2.72	36.88	10
sBP < 90	3.40	0.39	0.002	1.57	7.36	3
dBP > 90	2.70	0.65	0.129	0.75	9.70	3
RR > 40	18.21	0.95	0.002	2.83	116.95	18
Temp > 38	125.01	1.10	<0.001	14.43	108.31	125
CS (yes vs no)	5.85	0.42	<0.001	2.59	13.19	6
Number of CS	0.98	0.06	<0.001	0.97	0.99	1
PR > 120	4.14	0.40	<0.001	1.89	9.08	4
Validation model with total data set (n=5243)						
Parameters	**Odd ratio**	**S. E**	**Significance (p)**	**95% CI**		**Absolute risk***
				Lower	**Upper**	
sBP >140	15.50	0.31	<0.001	8.38	28.69	16
sBP < 90	2.09	0.20	<0.001	1.42	3.08	2
dBP > 90	0.89	0.30	0.706	0.50	1.61	1
RR > 40	23.19	0.47	<0.001	9.18	58.57	23
Temp > 38	55.90	0.46	<0.001	22.64	138.02	56
CS (yes vs no)	6.38	0.16	<0.001	4.71	8.65	6
Number of CS	0.98	0.00	<0.001	0.98	0.98	1
PR > 120	6.27	0.21	<0.001	4.14	9.50	6

*Absolute risk estimated by rounding the odds ratios to one significant figure

Although significant in the derivation model, high diastolic pressure (>90 mmHg) was not as much of a risk factor as the systolic BP, and this ceased to have significant

effect on SMO risk in the two validation data sets (**Table 3**). When interactions were considered, the diastolic blood pressure was found to be strongly collinear (correlation coefficient, r = 0.95) with systolic blood pressure, therefore diastolic BP was dropped in the proposed EWS monitoring chart (**Annex 5A**). When applied in the validation data sets, all other variables in the original model produced consistent effect in the same direction with variation in effect sizes (**Table 3**). Similarly, the clinical variables with the highest risk of SMO in the two validation models were fever and tachypnoea, with absolute risks of 125 and 18 respectively in the first validation model, and 56 and 23 respectively in the validation model with the complete case and control data.

5.6.4. Predictive accuracy for SMO

The final early warning system model from the derivation data set explained 66% of the variability in SMO with an area under the ROC curve of 92% (**Table 5.4**, **Annex 5B**). Given that the cases data set provides an already categorized (binary) clinical variables, diagnostic accuracy of the models was assessed based on number of parameters required to predict SMO with best screening properties. Using presence of five or more triggers as cut-off point to define SMO, the model predicted SMO with sensitivity of 86%, specificity of 92%, positive and negative predictive values of 84% and 93% respectively (**Table 5.4**). The first validation model produced very similar screening characteristic and discriminatory ability (AUROC 92%) (**Table 5.4**, **Annex 5C**). Not surprisingly however, the model with all cases and controls produced the highest positive predictive value (94%), but significantly reduced negative predictive value (61%). This was expected given the high prevalence of the outcome measure in the data set (case: control = 4:1). The model explained 58% of the variability in SMO with 92% discriminatory ability (AUROC 82%) (**Table 4**, **Annex 5D**).

Table 5 4 Predictive accuracy of the early warning system models (best performing cut-off 0.6)

Model	Sensitivity (95%, CI)	Specificity (95%, CI)	PPV (%) (95%, CI)	NPV (%) (95%, CI)	AUROC (95%, CI)	Negelkerke R^2
Original model (n=600)	86 (81-90)	92 (89-94)	84 (79-89)	93 (90-95)	0.92 (0.90-0.95)	0.69
Internal validation 1 (n=600)	81 (76-86)	90 (87-93)	81 (75-85)	90 (87-93)	0.92 (0.88-0.94)	0.69
Internal validation 2 (n=5243)	91 (90-92)	71 (68-74)	94 (93-95)	61 (58-64)	0.92 (0.9-0.95)	0.58

5.6.5. Proposed EWS chart

Measurements of temperature, pulse rate, systolic blood pressure, respiratory rate and delivery mode, in post-partum patients (caesarean delivery versus spontaneous vaginal delivery), constitute the primary early warning parameters from the three statistical models. Diastolic blood pressure was dropped as it was strongly collinear with systolic blood pressure (r = 0.95), and the latter was more clinically relevant and significant in all statistical models (**Table 5.3**). Consciousness level and low urine output (anuria) were dropped in the statistical models due to perfect prediction of outcome, not statistical significance. Therefore, the variables were forced into the proposed EWS chart adopting the AVPU (alert, responds to voice or pain and unresponsive) scale for consciousness level from the MEOWS chart recommended in the 2003-2005 CEMACH report (**Appendix 1A**, **Chapter 1**). Defining trigger as a single markedly abnormal observation (red trigger) or the combination of two simultaneously mildly abnormal observations (two yellow triggers), the corresponding values from the CEMACH MEOWS chart were converted into scores of 0 (normal observation), 1 (yellow trigger) and 2 (red trigger) in the proposed chart (**Annex 5A**). Mode of birth was scored as 0 and 1 for vaginal and caesarean births respectively. Inputs on the structural design of the chart were obtained from obstetricians (4 obstetricians CA, HA, MM and MI) and midwives (HM, TK, FM and FD), all from the academic team at the Centre for Maternal and Newborn Health, Liverpool School of Tropical Medicine (**Annex 1B**).

5.7. Discussion

We performed a multivariate logistic regression analysis using a case-control study design with clinical indices that were predictive of severe maternal outcome (deaths and near miss) using a stepwise approach to develop and validate a diagnostic predictive model for women admitted to all obstetric inpatient wards. To our knowledge, this analysis reports for the first time, the development and validation of a diagnostic prediction model and EWS for a general obstetric population in a low-resource setting using recommended methodology (Collins et al., 2015a).

A commendable effort was made previously by Carle and colleagues(Carle et al., 2013a) to develop an aggregate weighted early warning system that was specific for obstetric population. Given that the secondary data used in their analysis composed strictly of obstetric admissions to ICUs, generalizability of the derived model beyond this setting remain a major concern (McGlennan & Sherratt, 2013; Paternina-Caicedo et al., 2017; Smith & Prytherch, 2013). Similarly, computing fraction of inspired oxygen required to maintain SPO2 above 96%, being one of the EWS parameters, could be quite challenging in low-resource settings, as arterial blood gases measurement, or even pulse oximetry measurement equipment may not be readily available (Allegranzi B., 2015) (also results of **Chapter 4**: Feasibility study). Although fraction of inspired oxygen was not recorded in our case data, low SPO2 was not found to be a significant predictor of SMO risk in our final model. Unfortunately, we were unable to externally validate the obstetric EWS by Carle and colleagues because the clinical variables in the SMO cases were collected as categorical (binary) variables in our data set.

We found that temperature >38^{o} C was the strongest predictor of SMO. This was similar to the finding by Ryan and colleagues (2015) (Ryan et al., 2017) but different from the findings of two other validation studies (Carle et al., 2013; Singh et al., 2012).

Our finding of high systolic BP as a predictor of SMO was consistent with the findings of two inpatient obstetric ward-based validation studies which used morbidity (Singh S et al, 2012) and ICU admission as outcomes (Ryan et al., 2017), and an EWS external validation study that had death as outcome (Paternina-Caicedo et al.,

2017). However, those findings were different from the development and validation study that used intensive care admission database with death as outcome (Carle et al., 2013). This difference is not surprising because the EWS developed and internally validated by Carle and colleagues (2013)(Carle et al., 2013) used data within 24 hours of admission into intensive care unit while the other studies used data from inpatients that had no obvious need for critical care.

Our report of significant association between SMO and severe tachypnoea, high pulse rate, high diastolic blood pressure, and low consciousness level was consistent with the findings from the ICU-based external validation study by Paternina-Caicedo and colleagues (Paternina-Caicedo et al., 2017).

We found a significantly increased risk of SMO among women who had caesarean compared to vaginal birth, and the variable remained an important predictor of SMO in all our models during development and serial validations. It could be argued that while other clinical parameters are dynamic features of the condition of the patient, caesarean section is an event that does not change. However, attempt to adjust all available potential confounding factors (the 15 significant clinical variables at univariate level with SMO; Table 5.2) was made, irrespective of these parameters, mode of delivery remained a significant predictor of SMO in our datasets. This informed our inclusion of the variable in the proposed EWS monitoring chart (**Annex 5A**). We however, acknowledge the need for external validation especially in a setting with potential confounding factors other than those in our study cohorts (Collins et al 2015).

Our model has an excellent predictive ability to discriminate women who developed severe maternal outcome from those who did not (AUCs consistently above 90%). The model attained similar diagnostic predictive accuracy as one developed, internally validated (Carle et al., 2013a) and externally validated (Paternina-Caicedo et al., 2017) using data from obstetric intensive care unit patients. Our model also performed similar to non-obstetric cardiovascular, adult critical care and neonatal critical care score system developed (Knaus et al, 1981; Knuiman & Vu, 1997; Richardson et al, 2001). Compared to other routinely used EWS in obstetric ward settings, our model has significantly better screening

characteristics (positive predictive value of 94%, 95% CI 93-95), compared to an average of 41% reported for 16 different EWS versions (Umar A et al., 2019). This is of particular significance, since an early warning system that generates many false positive findings may possibly worsen clinical care, constitute a nuisance alarm by creating an excessive burden on the health system (Friedman et al*.,* 2015; Goldhill et al*.,* 2005). Potentially, the proposed chart presents an opportunity to institute life-saving interventions to improve clinical outcome. However, current evidence suggests that the use of EWS by itself is not enough to improve health outcomes, and that for this tool to perform optimally, an EWS must be integrated with an outreach support system, such as a rapid response team (Hillman, 2005; Umar, A., et al*.,* 2019).

Of the seven parameters in the proposed EWS chart from our analysis (**Annex 5A**), five (temperature, pulse rate, systolic blood pressure, respiratory rate and consciousness level) were included in majority (>80%) of the EWS published to date (Umar, A., et al., 2019). Delays in triage (identification of who is, or may become, severely ill and should be provided with a higher level of care) is believed to contribute immensely to increased burden of adverse obstetric outcomes in these settings (Gabrysch & Campbell, 2009). This is further confounded by unavailability of patient monitoring devices and other diagnostic equipment, especially in the primary healthcare settings (Allegranzi B, 2015). Therefore, in addition to the inpatient obstetric wards, we believe the proposed monitoring chart can present a potentially useful triaging tool to aid timely referral in primary healthcare centres in low- and middle-income countries. However, a prospective external validation study is recommended to assess effectiveness of the EWS developed in both primary, secondary/tertiary care in other low-resource settings to further substantiate these recommendations.

The major strength of this analysis lies in the robust maternal death and near-miss case data set which was prospectively collected primarily for research purpose with very few missing data (2.7% of participants), our strict adherence to diagnostic predictive model development process and reporting as recommended by TRIPOD (Collins et al., 2015). Additionally, a common limitation of EWS validation studies

was addressed in our analysis. This is the lack of standardization of outcome measures, which is especially common with studies using morbidity as outcome measure, as often, this was defined based on consensus rather than standardized definitions (Umar, A., et al*.,* 2019).

There are several limitations to this analysis. Firstly, SMO cases data consisted of already categorized clinical variables. Although cut-offs were based on recommendations for defining specific disease conditions (such as high blood pressure) by policymaking organizations like the WHO, it was not possible to validate different trigger thresholds for the model parameters. Secondly, lack of continuous data also made it impossible to externally validate other EWS versions like the CEMACH MEOWS (CEMACH, 2007) and the ICU-based chart developed by Carle and colleagues (2013)(Carle et al., 2013a). Additionally, pulse oximetry was poorly recorded in our study data set, especially in the controls where the parameter was assumed to be above 90%. Although absence of oxygen saturation could make our proposed chart more feasible to use in low-resource settings, evidence from other analyses has shown that it is a valuable predictor of death and serious obstetric complications (Cuthbertson et al*.,* 2007; Millman et al., 2011; Payne et al*.,* 2014; Von Dadelszen et al*.,* 2011). It is therefore probable that this clinical variable would still contribute to a statistically developed and validated EWS decision tool in our study population. This can be investigated in an appropriately designed study in future.

5.8. Chapter summary

Chapter 5: Design and validation of EWS

- The development and validation process of a simple obstetric diagnostic prediction model and EWS for use in resource-limited settings was presented in this chapter. The chapter also covers third objective of this PhD research.
- A multivariate logistic regression analysis was conducted using a case-control study design with clinical indices that were predictive of SMO
- Cases were 4360 women diagnosed with SMO, controls were 1000 obstetric admissions without SMO diagnosis between June 2012 and mid-August 2013
- Clinical observations collected within 24 hours of occurrence of SMO for cases, or birth in controls were used in the analysis.
- A combined data set was created with two controls per case and split randomly into development (n=600) and validation (n=600) data sets.
- Model's validity assessed using sensitivity and specificity, performance in predicting SMO assessed using receiver operator characteristic (ROC) curves.
- The final derived model was fitted on the validation data sets to assess its performance
- The model was converted into a simple score-based EWS using reference range proposed in the CEMACH MEOWS.
- Final model consisted of abnormal systolic blood pressure (SBP>140 mm Hg or <90 mmHg), high diastolic blood pressure (>90 mmHg), respiratory rate (RR>40/min), temperature (>38^{o}C), pulse rate (PR>120/min), caesarean birth, and number of previous caesarean births.
- The model was 86% (95% CI 81-90) sensitive and 92% (95% CI 89–94) specific in predicting SMO with area under ROC curve of 0.92 (95% CI 0.90–0.95).
- All parameters were significant in validation models except diastolic blood pressure which was dropped because of collinearity (r=0.95) with systolic blood pressure.
- The model maintained good discriminatory power across all validation data sets (AUC>90%) and had good screening characteristics
-

5.9. Conclusion

To the best of our knowledge, this analysis provides for the first time, an internally validated statistically developed diagnostic predictive model for all women admitted to obstetric wards in a low-resource setting. This model was used to develop a simple score-based EWS chart that has easy to measure parameters with readily available patient monitoring tools, hence constituting a potentially useful triaging tool in low-resource healthcare settings. Further work is however needed to validate this proposed chart externally in the obstetric wards as well as primary healthcare settings.

Chapter 6: Implementation and evaluation

6.1. Overview of the chapter

Building on the developed and internally validated EWS chart in the previous chapter, this chapter describes the last phase of the PhD project. In this phase, the EWS monitoring chart was implemented in a different cohort of obstetric patients using a longitudinal mixed-method (quantitative and qualitative) study design to evaluate its effectiveness and explore the experience of its use. The chapter provides a brief background leading to the objectives of the phase, then describes the study design and rationale for data collection methods used. Thence, it details how the sample size was calculated and participants were recruited in both the intervention and control arms of the study. Subsequently, data collection is discussed in detail along with measures taken to audit data and ensure quality throughout the data collection period. Thereafter, the data management and analysis are presented as well as the findings from both quantitative and qualitative components of the third phase of this PhD. Finally, the chapter concludes with a summary of the main points.

6.2. Background

Several EWS have been developed for obstetric patients, but the majority are the result of a clinical consensus rather than through statistical analyses, or were created using data from patients admitted to intensive care units (ICU), limiting their generalizability to non-ICU settings (Carle et al., 2013a; Hedriana et al., 2016b; Isaacs et al., 2014; Mhyre et al., 2014b; Paternina-Caicedo et al., 2017; Shields, 2016; S. Singh, Mcglennan et al., 2012).

The Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement recommends that new prediction models are tested on data used in its development (internal validation) and other data not used (external validation) (Collins et al., 2015a).

Therefore, secondary data on obstetric inpatients admitted to 42 Nigerian tertiary hospitals were used to develop and internally validate a simple obstetric diagnostic prediction model. This EWS was developed using recommended methods and is

suitable for use in resource-limited settings (details in **Chapter 5**: Design and internal validation of EWS model) (Collins et al., 2015; Umar, A., Manu, A., et al., 2019). The EWS model performed excellently in predicting severe maternal outcome (SMO: maternal death or near miss) in the derivation data set, with AUROC consistently above 90%, and demonstrated its potential for usefulness in other, similar settings.

This chapter covers the implementation and evaluation of usefulness of the developed EWS monitoring chart in a tertiary university teaching hospital in Nigeria.

6.3. Phase objectives

General aim

The aim of the third phase of the PhD project was to implement and evaluate the use of obstetric EWS as part of the extended emergency obstetric care (EmOC) (assisted vaginal delivery, caesarean section and perioperative care) training for quality improvement in the intervention hospital (University of Ilorin Teaching Hospital, Nigeria).

Specific objectives

a) To assess the effectiveness of obstetric EWS in improving measured patient outcomes using quantitative research methods.
b) To explore the experience and challenges of implementing the EWS among healthcare staff using qualitative research methods.

6.4. Methodology

6.4.1. Hypothesis

The hypothesis was that the EWS developed will perform equally well in a different setting from that of its derivation population. We also hypothesized that the EWS chart will provide an easier, more convenient and efficient alternative patient monitoring method to healthcare workers than current routine practices in the same setting.

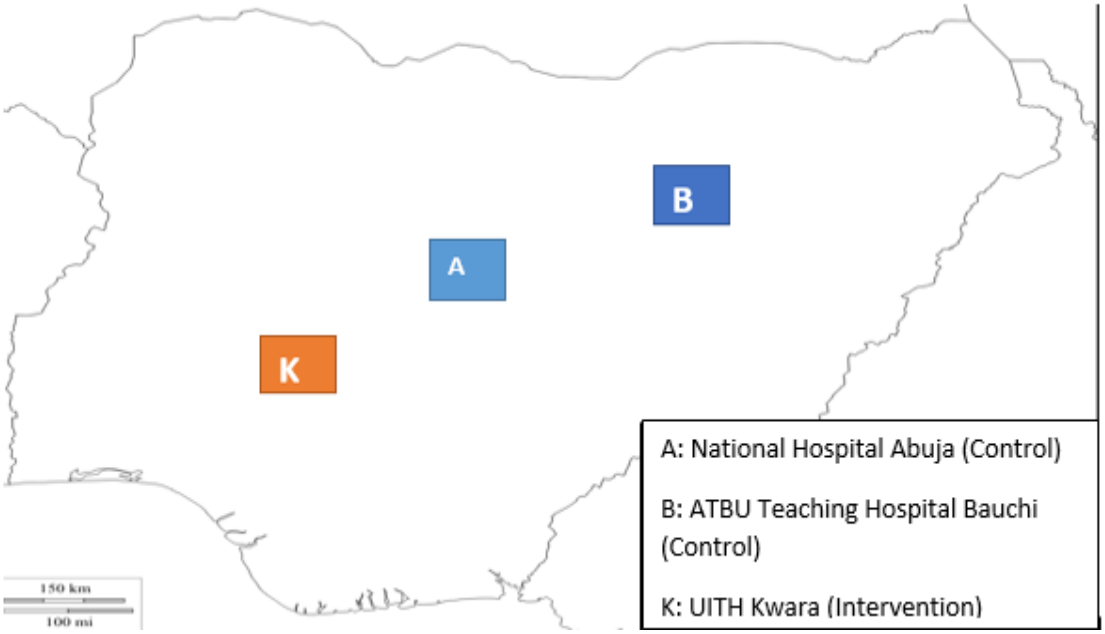
6.4.2. Study design

We employed a mixed-method design consisting of a controlled before–after quasi-experimental trial and qualitative interviews/focus group discussions to achieve both study objectives.

6.4.3. Setting

The study was conducted in three tertiary hospitals in the North-east, North-central and North-west parts of Nigeria, where the burden of adverse maternal outcomes is highest. One teaching hospital (University of Ilorin Teaching Hospital) was recruited as the intervention site and two other teaching hospitals, National Hospital Abuja and Abubakar Tafawa Balewa University Teaching Hospital Bauchi (ATBUTH), were recruited as control sites.

Figure 6 1 Map of Nigeria showing the phase 3 study sites



6.4.4. Description of the intervention hospital

The intervention was implemented in University of Ilorin Teaching Hospital, which was not part of the feasibility study- choice of this facility was purposive, as the centre for maternal and newborn health, LSTM where this PhD is supervised has a long-term partnership with UITH. Additionally, UITH is the intervention site for the CMNH's Johnson & Johnson's grant (charity number 222655) project for improving the quality of care of maternal and newborn health (MNH) in Kwara state, Nigeria. The hospital is a tertiary health care centre located in the north-central region of Nigeria. It receives patients from Kwara State as well as Kogi, Niger, Ekiti, Osun, and Oyo States. It is a multispecialty hospital providing specialist care in Neurosurgery,

Cardiothoracic Surgery, Orthopaedic Surgery, Obstetrics and Gynaecology, Paediatrics, and Internal Medicine, as well as other areas of specialty. It has a total space of 600 beds.

The Obstetric Unit of the hospital is housed in a two-storey building with a total space of 128 beds. It consists of antenatal and postnatal wards that have 30 beds each, a 25-bed postnatal surgical ward, an 18-bedded emergency ward, and a 25-bed gynecology ward. There are antenatal clinics, labor ward, ultrasound room, family planning unit, an operating theater with two functional suites, and a neonatal intensive care unit adjoining the labor ward. The Obstetrics and Gynaecology Department has four firms that are run by consultants who supervise the resident doctors and interns.

As part of the preparatory activities during the EmOC training in August 2018, baseline data was collected on the obstetric admissions, maternal deaths and direct obstetric complications over a 3-month period. This is to enable the design and sample size estimate of the study. As with other secondary data collected in the feasibility study, the baseline data was collected by the co-PI from labour ward register and obstetric department's monthly summaries in the intervention hospital. The data is presented below (**Table 6.1**)

Table 6.1: Baseline data in the intervention hospital (Dec 2017 to Feb 2018)

Months	Admissions	Deaths	Direct Obstetric complications	Sum
Dec 17	229	1	50	51
Jan 18	189	1	59	60
Feb 18	161	2	46	48

6.4.5. Participants

Pregnant and post-partum women admitted to inpatient wards with complications developing antepartum or during the puerperium (42 days post-partum) were eligible for inclusion. Women were excluded if they were in active labour, had met any of the three maternal near-miss criteria before hospital admission (clinical, management-based and organ-dysfunction-based criteria) (Say et al., 2009), or they were admitted straight to intensive care units without going through any of the other

inpatient wards. Participant eligibility for the qualitative interviews and focus group discussions is discussed under **Section 4.10**, below.

6.4.6. Intervention

The intervention is the use of obstetric EWS. The EWS chart developed (**Annex 6A**: EWS chart) was introduced to replace the vital signs charts of all recruited participants in the intervention site. The EWS chart introduced was a simple score-based recording chart for the patient's vital signs. It consisted of seven clinical parameters (temperature, pulse rate, respiratory rate, systolic blood pressure, diastolic blood pressure, consciousness level (based on the AVPU (alert, voice, pain and unresponsive) scale) and mode of birth for post-partum patients). These parameters were scored as 0 for normal, 1 for mild and 2 for severe derangements, as previously reported in **Chapter 5** (**Annex 6A**: EWS chart). An escalation protocol at the top-right corner of the chart guides frequency of patient monitoring and when to trigger clinician's review (**Annex 6A**: EWS chart); scores of 0 or 1 are reassuring, hence requiring 12-hourly monitoring or as usual for post-operative patients. For a score of 2, observations need to be repeated after 30 minutes; if it remains the same or rises, the clinician needs to be informed to review it. Patients scoring 3 or higher are likely to deteriorate clinically and require immediate review by a clinician.

The two control sites were to continue with the existing practices of patient monitoring.

6.4.5. Sample size calculation

Baseline data for the intervention site indicate that the average monthly number of obstetric admissions was 190; of these, approximately 25% to 30% experience a maternal death or direct obstetric complications (pre-eclampsia/eclampsia, antepartum haemorrhage, postpartum haemorrhage, sepsis, obstructed labour, abortions complications, ectopic pregnancy and thromboembolism) The table below indicates proportion reduction that could be detectable with 80% or 90% power for a follow-up period of between three and six months.

Table 6 1 Sample size estimate in the intervention arm

		Baseline of 25%		Baseline of 30%	
Number in pre-intervention	**Number in the follow-up period**	**Reduction detectable**		**Reduction detectable**	
		80% power	**90% power**	**80% power**	**90% power**
380 (2 months)	570 (3 months)	8.0%	9.1%	8.6%	9.8%
	760 (4 months)	7.6%	8.7%	8.1%	9.3%
	950 (5 months)	7.3%	8.4%	7.8%	9.0%
	1140 (6 months)	7.1%	8.2%	7.6%	8.8%
570 (3 months)	570 (3 months)	7.2%	8.2%	7.7%	8.8%

Table 6.1 shows reductions detectable from baseline 44prevalence (not reduction to the displayed figures).

The additional month pre-intervention increases the power to detect a specified difference and reduces the total number of months for which data needed to be collected for a given reduction to be detectable. We therefore considered a three-month period for each of the pre- and post-intervention follow-ups. Factoring in a possible exclusion rate of around 5%, the sample size considered was 1200 in the intervention site (600 each pre- and post-intervention). The same number of participants were to be recruited in the control sites, as illustrated in **Table 6.2**, below.

Table 6.2 Breakdown of sample size by study arms

Study arm	**Before**	**After**	**Total**
Intervention	600	600	1200
Control 1	300	300	600
Control 2	300	300	600
Total	1000	1000	2400

Intervention = UITH Ilorin, Control 1 = National Hospital Abuja, Control 2 = ATBUTH Bauchi

6.4.6. Outcome measures

Primary outcomes

The primary outcome measure was SMO, which encompasses maternal death based on the ICD-10 definition and maternal near miss based on the three near-miss criteria (clinical, management-based and organ dysfunction) (Say et al., 2009). However, where data on nearmiss based on the three criteria is not available,

outcomes will be taken as direct obstetric complications as diagnosed by healthcare professionals.

Secondary outcomes

Secondary outcome measures considered were the rate of vital signs monitoring and recording (respiratory rate, pulse, blood pressure and temperature), duration of hospital stay, speed of post-EWS trigger specialist review, caesarean section rate and rate of instrumental delivery.

The details of primary and secondary outcomes are clearly defined in **Table 6.3**, below.

Table 6 3 Outcome measures and definitions

Outcomes	Definition
Maternal death	Death of a woman while pregnant or within 42 days of termination of pregnancy from causes related to or aggravated by the pregnancy or its management and not from accidental or incidental causes
Near-miss	A woman who nearly died but survived a complication hat occurred during pregnancy, childbirth or within 42 days of termination of pregnancy. This will be identified based on the clinical based, intervention-based and organ system dysfunction-based criteria as defined by Say et al(Say et al., 2009). Data collectors will be trained to correctly identify maternal near-miss cases based on these criteria.
ICU admission	The number of admissions to intensive care or high dependency care units that are due to direct obstetric conditions.
Vital signs recording	Rate of recording of respiratory rate, pulse, blood pressure and temperature computed as the ratio of the observed to expected recording frequency in percentage.
Duration of hospital stay	This is the average number of days spent between hospital admission and discharge.
C/S rate	This will be the proportion of births that are conducted via caesarean section
Instrumental birth rate	This will be the proportion of births that are conducted using vacuum extractor or forceps

6.4.7. Pre-implementation data collection

Based on the outcome measures described above, a baseline data-extraction sheet was constructed (**Annex 6B**: Trial data abstraction sheet) and coded into Android

data collection devices (ODK Collect). Three data collectors (research assistants) were recruited and trained for the baseline data collection. Medical record staff were allocated to assist in the identification and retrieval of management case notes across all three study sites (facilitated by the respective co-PIs). Following the defined eligibility criteria in **Section 4.4**, above, 600 folders were obtained in the intervention hospital for baseline pre-implementation data collection. Similarly, an equivalent number of folders were collected in the control facilities (300 per facility) for comparison. Folders included at baseline were for all eligible participants admitted to the three health facilities between 1st August and 31st October 2018.

In addition to records of the outcome measures (**Table 6.3**, above), other parameters were collected for comparison within and between study arms. These included age, weight and height, obstetric variables (parity, number of antenatal clinic visits, gestational age at the time of admission/birth, pregnancy outcome) and diagnosis.

6.4.8. Extended EmOC training

The extended EmOC training was an intensive multidisciplinary training course developed by CMNH LSTM, targeting obstetric surgical and anaesthetic providers. The training package addresses, 5 of the 8 components of the WHO framework for the quality of maternal and newborn health care (evidence-based practices, effective communication, respect and preservation of dignity, emotional support, ensuring competent human resources).

The short (5 days), onsite training package, has six modules (Labor ward leadership and management, Decision making in labour, Peri-operative care, Second stage of labour, Surgical obstetric interventions, and Post-operative care, discharge planning and clinical audits). These are delivered through 18 lectures and short training videos, 50 simulation-based sessions (workshops, simulations and role play, hands on training using low cost but high-fidelity mannequins). There is an emphasis on improving communication skills between staff and patients, in addition to enhanced team working using the WHO safe surgical checklist, clinical audits, and use of obstetric early warning charts (OEWS).

Since 2018, pilots and adaptations to the course have been carried out in Cambodia, Kenya based on feedback from the participants and faculty, and Nigeria have been used to refine and update the package. After training, participants demonstrated improved knowledge scores, particularly in the AVD (Kenya: n=17, 15.8% CI: 10.5, 21.1, Nigeria: n=42, 17.3% CI: 14.7; 19.9) and CS (Kenya: n=18, 14.3% CI: 11.1, 17.6, Nigeria: n=35, 21% CI: 18.5, 23.4) modules. Individual and team action plans developed at the end of the training included implementation of the obstetric EWS, the use of the WHO safe surgical checklist and improved communications with patients.

LSTM technical staff and senior faculty from UITH facilitated a one-week expanded EmONC training programme for medical doctors, nurses and midwives from 16 general hospitals and the UITH, including nurses/midwives who went on to use the EWS following its implementation. This training increased the capacity of the above cadres to assess indications for caesarean section, provide quality caesarean section, use anaesthesia safely, perform mid cavity and rotational vacuum vaginal deliveries and provide quality peri-operative care. Modified Early Warning Scores (MEOWS) was also introduced to reduce the risk of complications and death.

6.4.9. Trial procedure

After baseline data collection, the EWS chart was implemented in the intervention hospital. The implementation was part of the extended emergency obstetric care training (assisted vaginal delivery, caesarean section and perioperative care), which was a department-wide initiative for quality improvement. Training workshops on EWS were organized and delivered by local and UK-based consultants during the quality improvement sessions of the project in August 2018.

Routinely collected patient information was to be used for the research, hence no individual-level consent was deemed necessary as was performed in similar studies (Merriel et al*.,* 2017; Sheikh et al*.,* 2017; Singh, A., et al*.,* 2016).

The research component of the EWS implementation started with a courtesy visit by the principal researcher and the local co-PI of the intervention hospital to the hospital authorities. The authorities visited included the Chair Medical Advisory

Committee (CMAC), the Deputy CMAC, who was an obstetrician, and the head of the Obstetrics and Gynaecology department. A department meeting was organized with all clinical staff (including doctors, nurses and midwives) in the Obstetrics and Gynaecology department. A presentation was delivered by the principal researcher at this meeting on 12th November 2018, during which the design process of the chart and how it is used for patient monitoring were explained. Following this, circulars were distributed to all obstetric wards (emergency, antenatal, postnatal medical, postnatal surgical and gynaecology wards) directing ward heads to adopt the EWS chart in place of routine vital signs charts for all obstetric inpatients. A local implementation team was constituted by the co-PI. The team consisted of the primary researcher, a senior resident doctor (SI) and a junior resident doctor (SG). The team was reinforced by the Chief nursing officer in charge of the obstetrics and gynaecology emergency unit and the chief resident of the Obstetrics and Gynaecology department. The two participated in the EWS training, recruitment of research participants and surveillance, but did not take part in data collection.

All staff involved in the monitoring of obstetric patients were trained on the use of the chart by the local implementation team in batches. The training was conducted over a period of seven days in the 5 inpatient wards. Specifically, the team went round all wards to train the nursing staff (nurses and midwives) taking different clinical shifts (morning (8am to 2pm), afternoon (2pm to 10pm) and nights (10pm to 8am)). This way, we covered all the nurses/midwives that undertake patient monitoring in the obstetric unit.

The training focussed on how to score the seven EWS parameters and how these are computed into a single EWS score for each set of investigation. It was also explained during the training that scores of 0 or 1 would require a 12-hourly monitoring, for a score of 2, observation should be repeated after 30 minutes and if remains the same or increases, then this should be escalated to doctors. In cases where cumulative EWS score is 3 or above, immediate escalation should be done to doctors as per the EWS protocol. Management of specific complications were as per hospital protocol or usual practice as appropriate. All subsequent queries related to the chart were directed to the implementation team.

Patients were recruited on admission to all five obstetric inpatient wards by the ward nurses. The EWS charts were incorporated into the medical files of recruited participants, after which they were prospectively followed up until the end of their stay in hospital (discharge or demise) during which a dedicated research assistant (a medical intern doing obstetrics and gynaecology rotation) retrieved all completed EWS charts for analysis. Women in active labour were excluded and monitored with partograph as defined by the study protocol. Data collection was conducted until four months' post-implementation period (1st December 2018 to March 31st 2019) before the desired sample size (n=600) was achieved.

To assess any change in practice, the prevalence of outcomes (listed above in **Table 6.3**), was checked for trend effects or effects of other quality improvement programmes during the study period, and secondary data were collected in the control sites during the equivalent period after EWS implementation (1st December 2018 to 31st March 2019). All quantitative data were collected using Android data collection devices, after which they were extracted to a Microsoft Excel spreadsheet for analysis.

6.4.10. Qualitative interviews and focus group discussions

Semi-structured key informant interviews (KII) and focus group discussions (FGD) were conducted in the intervention hospital at the end of the follow-up period in April 2019. These activities were employed to explore the experience of health workers in the use of the early warning system.

The KIIs aimed to collect in-depth information on the perceptions of health workers of the usefulness of obstetric EWS charts and challenges that might have been experienced and how these might have been addressed. The participants were purposively selected but very experienced midwives/nurses in administrative positions and doctors in the Obstetrics and Gynaecology department. A standardized open-ended interview approach was employed in the early part of all interviews. Open-ended questions were designed to respond to the interview aims, and all the interviewees were asked the same questions (**Annex 6C**: KII topic guide). However, the interviewer pursued other, related subjects of interest deemed

relevant during the latter parts of the interviews as relevant themes emerged from the quantitative data.

The FGDs targeted staff nurses and midwives who conducted patient monitoring on the wards. By conducting the FGDs, we aimed to explore and understand the experiences of using the chart and challenges encountered from the viewpoint of those using the chart. Such rich data were also intended to allow for triangulation with data from KIIs.

Once identified, participants were oriented about the research and participant information sheets were issued by the principal researcher (**Annexes 6D1–2**: Participant information sheet and consent forms). All KIIs and FGDs were facilitated by the principal researcher (and a research assistant in the case of the FGDs), who had been trained on how to moderate sessions and had significant experience in conducting qualitative research. Informed consent, including consent to audio-recording of interviews/FGDs, was obtained from all participants prior to interviews and FGDs. If any participant refused consent to audio-recording of the interview, the facilitator (or research assistant in the case of FGDs) took notes only during those interviews or focus group sessions. All data collection continued until saturation was reached.

6.5. Quality control

Quality control was maintained throughout the research, by monitoring of the process, for both the quantitative and qualitative components of the research. The strategies employed to achieve this monitoring process include the following:

For the quantitative study (quasi-experimental trial), compliance was audited by the principal researcher and local implementation team during the immediate post-implementation period. Training of nurses and surveillance to check adherence started from the afternoon shift of Monday 12th November 2018. This task was undertaken by the principal researcher with the local implementation team and went on during all shifts (three times per day: morning, afternoon and evening shifts) until Friday 16th November 2018, when all obstetric inpatients had the EWS charts in place of their routine vital signs charts.

Thenceforward, the surveillance was continued by the local implementation team without the principal researcher at least twice per week, ensuring that the charts were correctly used on all research-eligible participants. Additionally, formal monthly audits were performed by the local implementation team on the last day of each calendar month to monitor the use of the chart and any ongoing change in practice. A quality indicator was adopted (**Annex 6E**: Quality audit checklist) (Merriel et al., 2017) to provide the implementation team with an easy yet objective way to assess the quality of the implementation. This indicator audited the EWS charts of all obstetric inpatients on a particular day in a month (usually the last working day of each calendar month). It captured the usage rate of charts (number of patients with correctly completed EWS charts/number of charts reviewed), whether healthcare staff took appropriate action on abnormal observations (number of cases in which action was taken/total number of charts requiring action), and the timeliness of the action if one was required (total number where action was taken within the required time frame/total number where action was taken).

For the FGDs and KIIs, a comprehensive and detailed standardized operating procedure manual guided data collection (manuscript in preparation for the study protocol, **Annex 6F**). Topic guides were pretested before their use in the full KIIs and FGDs and only relevant questions were asked, to avoid redundancy and ensure data efficiency.

Emphasis was placed on the trustworthiness of the research. The research aimed to ensure that participants felt comfortable and that they were able to express themselves or behave naturally (credibility), by ensuring that sufficient rapport was established between the researcher and the participants (Richie, J., Spencer, L., 2003). Efforts were made to ensure that the sample was representative of the study population, and data collection continued up to the point when no new information was being retrieved during the FGDs and KIIs (i.e., saturation was achieved).

6.6. Data management and analysis

6.6.1. Quantitative data

Quantitative data collected on Android devices (ODK Collect) were exported to a Microsoft Excel spreadsheet and cleaned for analysis. Data analysis was conducted using IBM SPSS version 23. Normality of distribution of variables was assessed by using distribution plots and Shapiro-Wilk testing. Cumulative and facility-specific characteristics were summarized by mean (SD) for continuous variables and percentages for categorical variables.

Descriptive statistics were calculated to evaluate the monthly recruitment rate in the study (number of recruited women compared to eligible women), the number of women with correctly completed observation charts, the number with observations that should have triggered action, the number of triggered women for whom action was taken, and the index of timeliness of the review.

Prevalence of outcomes during the post-implementation period at the control site was reported to check for trend effects or effects of other quality improvement programmes during the study period. Outcome measures were compared within and between study arms using independent sample t-testing and chi-square for continuous and categorical variables respectively. $P<0.05$ was considered as statistically significant. Results were presented in tables and charts. All quantitative data will be stored for a maximum of five years and will be destroyed afterwards.

6.6.2. Qualitative data

KII and FGD audio scripts were transcribed verbatim, ensuring all identifying information was removed and transcripts were anonymized. A thematic framework approach was employed to analyse the qualitative data.

Familiarization was carried out by repeated listening to the audio recordings. A thorough review of the raw data was carried out to identify important themes and concepts. These recurring themes were then sorted and grouped under a smaller number of broader categories of main themes and placed within an overall framework.

After a preliminary contextual framework was developed, “indexing” was performed, which entailed applying the initial framework to the raw data to check

how categories fitted. Modification of the framework was then performed where necessary, such as the addition of missing categories, following which the framework was appropriately labelled. These tasks were done electronically with the aid of computer-assisted qualitative data analysis software (CAQDAS), NVivo 12.

Subsequently, data were sorted by themes, and then reduced through summarization and synthesis (Richie, J., Spencer, L., 2003). A set of thematic matrices/charts were created, and each main theme and its associated subtopics were plotted on a separate thematic chart. Respondents were each allocated a row in the matrix, while each subtopic was displayed in a separate column. Key parts of each piece of data were summarized and placed appropriately in the thematic matrix (charting). Throughout the charting process, an attempt was made to maintain a balance between reducing the data and preserving the context, and the language in which it was expressed.

Having finished the qualitative data management steps of the framework analysis, we tried to make sense out of the synthesized evidence using descriptive accounts (Richie, J., Spencer, L., 2003). Emerging understandings were tested, alternative explanations were sought and results were presented.

6.7. Results

6.7.1. Characteristics of the study settings

The three teaching hospitals were located in urban areas in northern Nigeria. During the seven-month period of the study (1st August 2018 to 31st March 2019, excluding November 2018), 4258 women were admitted for pregnancy complications or childbirth. Bauchi recorded the highest volume of obstetric admissions at 2229, compared to National Hospital Abuja, which had the lowest (712). Overall, 3997 live births and 273 stillbirths were recorded in the three facilities, placing the overall LBR and SBR at 93.4% and 64.6/1000 births respectively. At facility level, Bauchi had the highest SBR (88.4/1000), followed closely by Ilorin, having 71.2/1000, with Abuja having the lowest at 34.2/1000 (**Table 6.4**). Nearly one in five births was preterm (before 37 completed weeks of gestation). The highest preterm birth rate

was seen in Abuja at 23.6%. Despite having more births than the two other hospitals, Bauchi reported the lowest prevalence of preterm births at 8.3%.

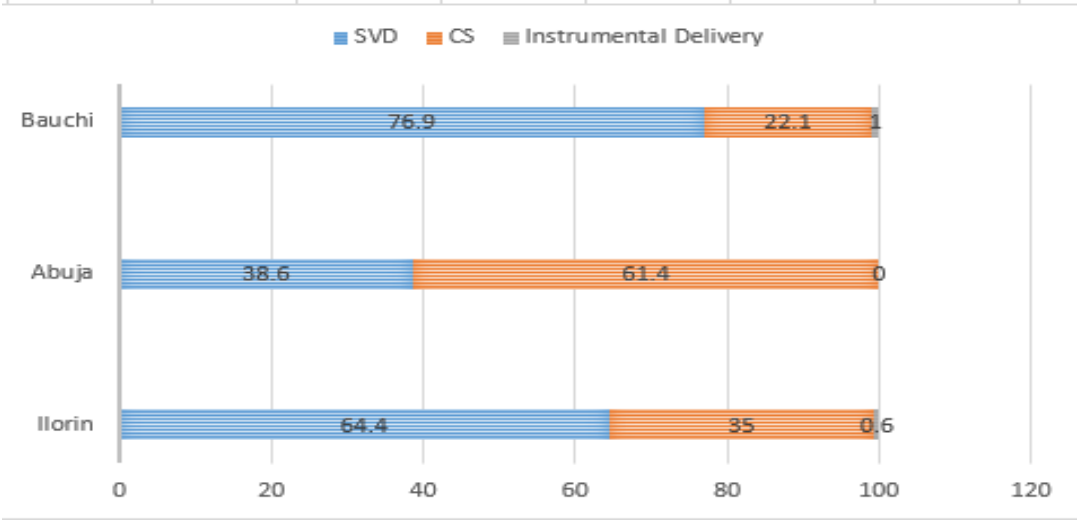
Table 6 4 Baseline characteristics of the three study hospitals

Characteristic	Ilorin	Abuja	Bauchi	Overall
Total admissions	1317	712	2229	4258
Stillbirth rate /1000	71.2	34.2	88.4	64.6
Preterm rate (%)	194 (14.7)	166 (23.6)	216 (8.3)	576 (12.4)
Vaginal births (%)	851 (64.4)	271 (38.6)	2003 (76.9)	3125 (67.6)
Caesarean births (%)	463 (35.0)	431 (61.4)	575 (22.1)	1469 (31.8)
Vacuum births (%)	7 (0.5)	0 (0.0)	21 (0.8)	21 (0.6)
Forceps births (%)	0 (0.0)	0 (0.0)	4 (0.2)	4 (0.1)
Institutional MMR	1393	442	1320	1052

6.7.2. Modes of birth

Overall, 67.6% of all births in the three facilities were spontaneous vaginal, while the cumulative caesarean section (C/S) rate was 31.8%. In terms of the total number of births, Ilorin and Bauchi had significantly more births during the study period than Abuja. However, by proportion, Abuja had a caesarean section rate (61.4%) nearly three times higher than Bauchi's, which was just 22%, and almost twice as much as Ilorin's at 35% (**Table 6.4**; **Figure 6.2**).

Figure 6 2 Modes of birth (%) in the three study facilities



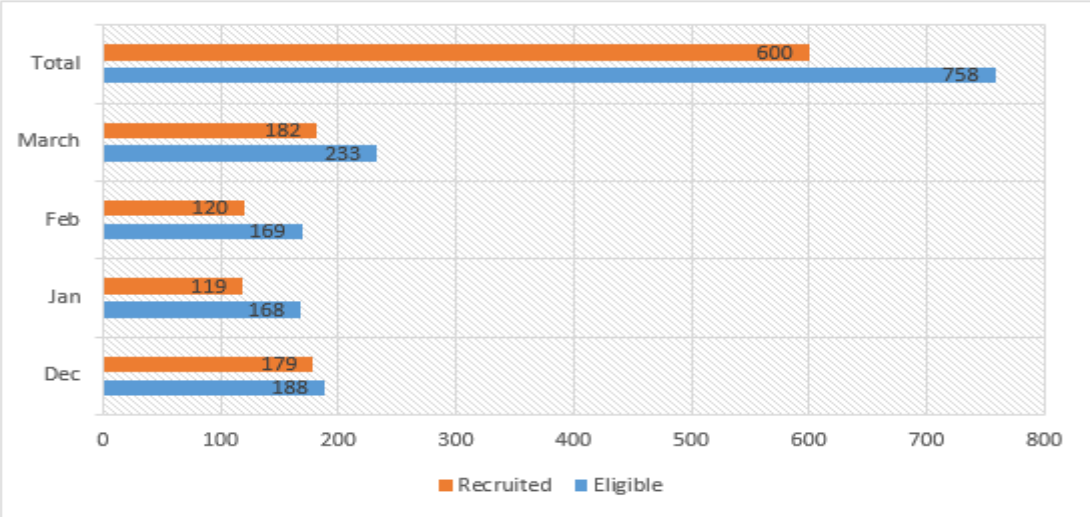
Instrumental delivery rate was almost negligible in all three hospitals (**Figure 6.2**). No vacuum deliveries were conducted in Abuja, while Ilorin and Bauchi reported vacuum delivery rates of 0.5% and 0.8% respectively. Similarly, only four (0.2%) forceps deliveries were conducted in Bauchi during the seven-month period of this study, while none was reported in Abuja or Ilorin (**Table 6.4**; **Figure 6.2**).

6.7.3. Recruitment

During the baseline pre-implementation period (1st August to 31st October 2018), 1200 women were recruited into the study retrospectively, consisting of 600 in the intervention arm (Ilorin), and 300 each in the two control arms (Abuja and Bauchi). EWS was implemented from 12th November 2018. A transition period of two weeks was allowed to audit implementation before the recruitment of research participants was commenced for prospective post-implementation data. Following surveillance by the local implementation team, a target of 100% implementation among all obstetric admissions to five inpatient obstetric wards (gynae emergency, antenatal, postnatal medical, postnatal surgical and gynaecology wards (for spillover obstetric admissions)) was achieved by 26th November 2018.

Recruitment started from 1st December 2018 in Ilorin, during which the highest recruitment rate of 95.2% was reported. However, the recruitment rate fell significantly in January, when only 70.8% of research-eligible patients were recruited into the study, but rose steadily thereafter, reaching a peak of 78.1% by the end of March 2019. Overall, sample size (n=600) was achieved after four months (1st December 2018 to 31st March 2019), with an average recruitment rate of 78.8% (**Figure 6.3**). Participants were recruited retrospectively in the two control arms (n=600, 300 in each facility) using convenience sampling matching for the duration of admission (December 2018 to March 2019) and eligibility criteria.

Figure 6 3 Recruitment of participants in Ilorin (1st December 2018 to 31st March 2019)



6.7.4. Characteristics of study participants

General characteristics

Table 6.5 illustrates the characteristics of the study participants. There was no difference between the ages of the women in the intervention and in the control groups at baseline (p=0.348) and post implementation (p=0.169). Although they had similar heights, participants in the intervention group weighed significantly more at baseline (p=0.038) and during the post-implementation period (p=0.023). More women were registered for antenatal care in the control hospitals at baseline (p=0.024); however, this difference ceased to be significant in the post-implementation cohort (p=0.155). There was no difference in parity or age at which women registered for antenatal care, but, overall, women in the control arm had more frequent antenatal visits than participants in the intervention arm (**Table 6.5**).

Table 6 5 Characteristics of study participants

	Baseline (n=1200)			Post-implementation (n=600)		
Characteristic	**Intervention** (n=600)	**Control** (n=600)	***P-value***	**Intervention** (N=600)	**Control** (n=600)	***P-value***
Age (years)	30.0 (5.3)	28 (6.4)	0.348	30 (5.2)	28 (6.3)	0.169
Weight (kg)	72.0 (14.4)	63 (14.2)	**0.038**	70 (11.7)	62.7 (13)	**0.023**
Height (m)	1.61 (0.05)	1.58 (0.09)	0.673	1.6 (0.06)	1.6 (.09)	0.334
*LOS (days)	3.6 (3.2)	2.4 (1.8)	0.368	3.7 (3.5)	2.3 (1.6)	0.714
Booked (%)	60.8	72.2	**0.024**	65.7	68.4	0.155
Booking GA (days)	24.8 (8.4)	25.5 (8.1)	0.906	24.6 (8.4)	25.1(8.1)	0.531
ANC visits	2.6 (1.3)	4.3 (2.3)	**0.036**	2.7 (1.7)	4.4 (2.3)	**0.042**
Parity	2.2 (1.4)	2.9 (2.3)	0.305	2.2 (1.3)	3.0 (2.3)	0.181

LOS: Length of hospital stay; Booked- patients registered for ANC; Booking GA- Gestational age at ANC registration

Completion rate of EWS chart

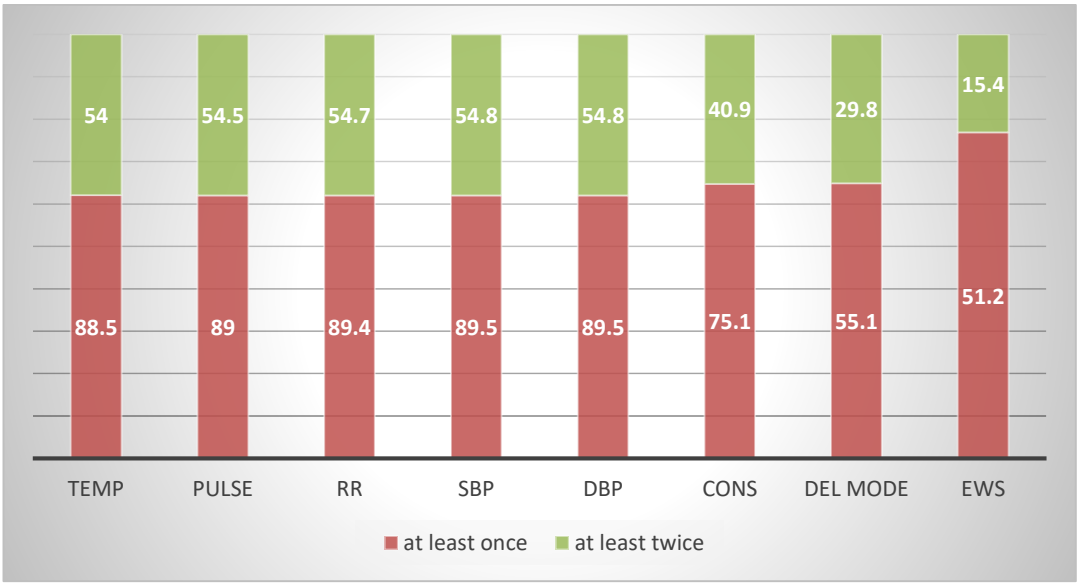
Following the implementation of the EWS chart in the intervention hospital (December 2018 to March 2019), data were extracted from the EWS charts for all recruited participants (n=600) at the end of hospital stay for analysis.

According to the EWS escalation protocol, all clinically stable obstetric patients (EWS score of 0 or 1) should have seven EWS chart parameters (temperature, respiratory rate, pulse rate, systolic blood pressure, diastolic blood pressure, level of consciousness and delivery mode) monitored and documented twice in 24 hours. Frequency of monitoring increases with acute deterioration based on EWS scores. A single pre-trigger EWS score (score of 2) necessitates repeated vital signs monitoring in 30 minutes. Two consecutive pre-trigger scores or EWS score of 3 and above (at any point during patient monitoring) indicates an urgent need for clinical review by a doctor.

Overall, recording of EWS parameters was incomplete, with regular monitoring (at least twice in 24 hours) of temperature, pulse, respiratory rate and blood pressure performed in 54% of the study participants (**Figure 6.4**). Most patients (over 80%) had all vital signs monitored and recorded at least once in 24 hours. The least frequently recorded EWS parameter was mode of birth for post-partum patients, which was recorded at least once daily in just over half (55%), and regularly in only about a third (29.8%), of the study participants.

Although monitored and recorded, EWS parameters were converted and summed into an EWS score in significantly fewer patients; only 15.4% (n=92) of the study participants had EWS scores documented as prescribed by the study protocol (at least twice in 24 hours). About half of the study participants (51.2%, n=307) had EWS scores recorded at least once in 24 hours (**Figure 6.4**).

Figure 6 4 Completion rate of the EWS parameters (% per 24 hours)



EWS trigger system

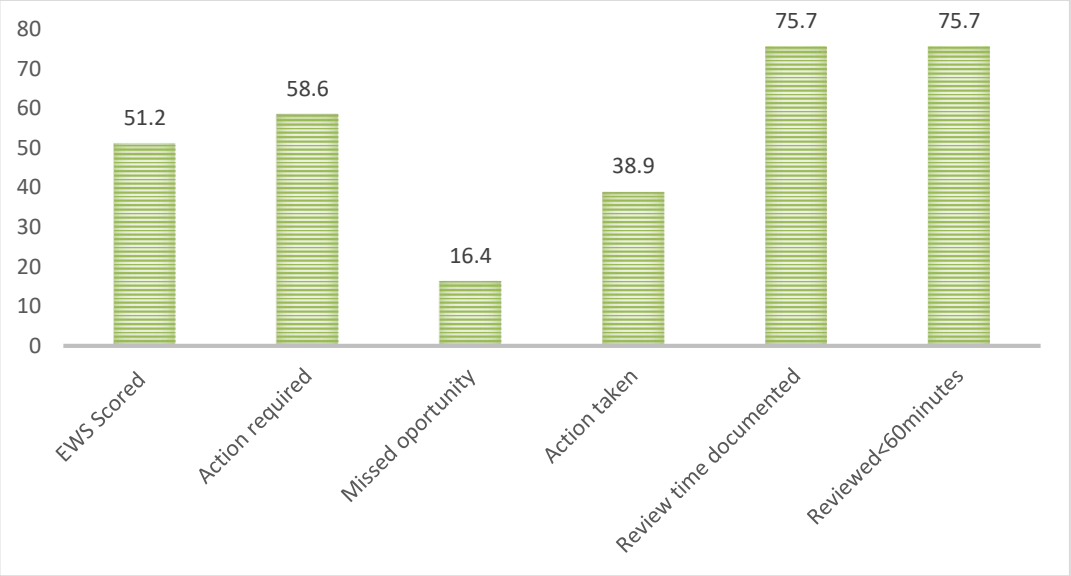
During the four-month follow-up period after the EWS implementation in the intervention hospital, about 58.6% (n=180) of the 307 women who had EWS score documented at least once in 24 hours required medical review by a doctor (**Table 6.6**). Of these, 38.9% (n=70) were reviewed by a doctor. In terms of timeliness of the review, about three quarters of the reviewed patients (75.7%, n=53) had the time of doctor's review correctly documented on the EWS chart; all of these patients were reviewed within 60 minutes, as recommended by the EWS escalation protocol.

Table 6 6 uptake rate of EWS in the post-implementation period (n=600)

Parameter	Frequency (n=600)	Proportion (%)
EWS scored	307	51.2
Action required	180	58.6
Missed opportunity	48	16.4
Action taken	70	38.9
Review time documented	53	75.7
Reviewed < 60minutes	53	75.7

By converting the recorded EWS parameters of the unscored patients (49.8%, n=293) into a corresponding score, and calculating the cumulative EWS scores based on the scoring guideline, it was noted that 48 patients (16.4%) would have required a medical review. None of these patients were reviewed by a clinician, hence this being referred to as a missed opportunity (**Table 6.6**; **Figure 6.5**).

Figure 6 5 uptake rate of EWS in the post-implementation period (n=600)



Maternal morbidity

Overall, maternal morbidity rate was higher in the intervention hospital. The difference was especially significant in the cases of obstetric haemorrhage, sepsis, obstructed labour and abortion. During the baseline pre-implementation period, twice as many women suffered obstetric haemorrhage in the intervention hospital compared to the controls. Similarly, the prevalence of obstructed labour and abortions in the intervention arm was twice that of the control hospitals. The commonest obstetric complication was sepsis, which complicated 12.2% and 8.8% of the obstetric admissions in intervention and control hospitals respectively. Although prevalence of both hypertensive disorders and prolonged labour were higher in the intervention compared to the control arms, the difference did not reach statistical significance, nor did the difference in ICU admission rates (**Table 6.7**).

Similar distribution of maternal morbidity was seen across study arms in the post-implementation period (**Table 6.7**); patients were three times more likely to suffer obstetric haemorrhage or abortions, and twice as likely to have obstructed labour

in the intervention hospital compared to the controls. Sepsis also remained the commonest complication, affecting 12.7% and 8.7% of obstetric admissions in the intervention and control hospitals respectively (**Table 6.7**).

Table 6 7 Prevalence of maternal morbidity

Baseline period (1st August to 31st October 2018)			
Condition	Intervention (n=600)	Control (n=600)	Chi-square P-value
Haemorrhage (%)	10.7	5.2	**0.027**
Sepsis (%)	12.2	8.8	**0.044**
Hypertensive disorders (%)	10.5	7.5	0.125
Prolonged labour (%)	10.3	7.7	0.472
Obstructed labour (%)	9.8	4.3	**0.018**
Thromboembolism (%)	0.3	0.0	NA
Abortions (%)	5.8	2.5	**0.023**
ICU admission (%)	0.2	0.4	0.993
Post-implementation period (1st December 2018 to 31st March 2019)			
Haemorrhage (%)	11.1	4.9	**0.019**
Sepsis	12.7	8.7	**0.040**
Hypertensive disorders	9.8	7.6	0.331
Prolonged labour	10.4	8.0	0.533
Obstructed labour	9.8	5.8	**0.049**
Thromboembolism	0.2	0.0	NA
Abortions	6.4	2.4	**0.040**
ICU admission	0.3	0.5	0.916

Institutional maternal mortality

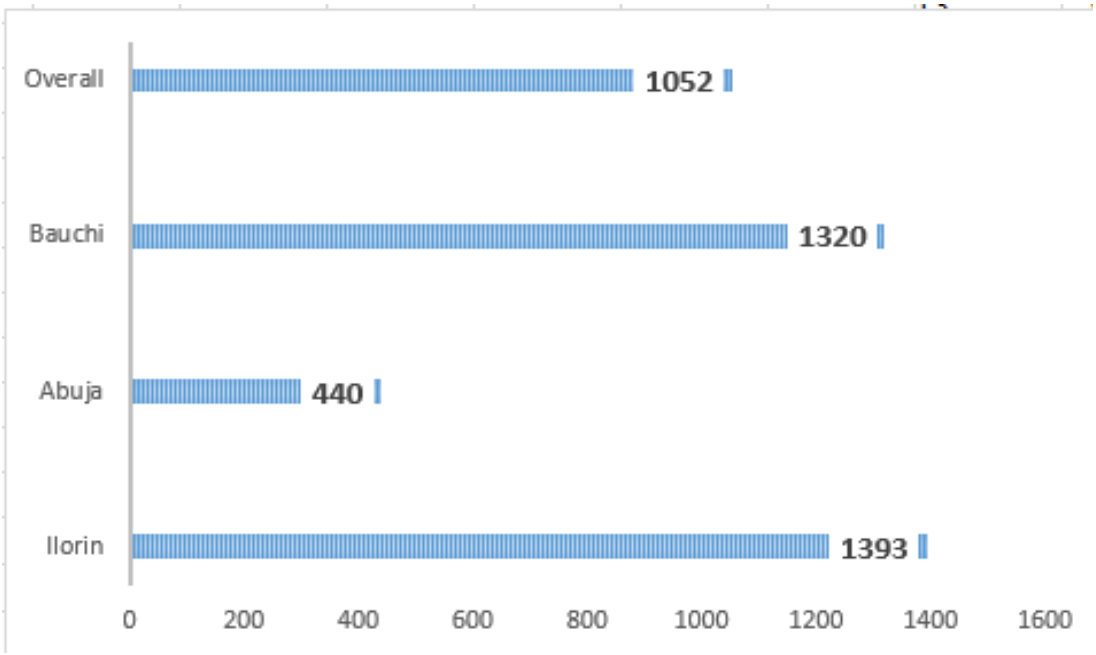
Fifty women died due to causes related to pregnancy or childbirth across the three health facilities, putting the cumulative estimated MMR at 1052 per 100,000 live births (**Table 6.4**). Facility-level estimates showed a similar prevalence of maternal death in Ilorin and Bauchi (institutional MMR of 1393 and 1320 per 100,000 live births respectively), both having over three times as many deaths as Abuja (institutional MMR of 440 per 100 000 live births) (**Table 6.8**; **Figure 6.6**).

Table 6 8 Institutional MMR in the three study health facilities

Characteristic	Ilorin	Abuja	Bauchi	Cumulative
MMR	1393	440	1320	1052

MMR- maternal mortality ratio

Figure 6 6 Institutional MMR in the three study health facilities



Causes of maternal death

Table 6.9 elucidates the causes of maternal mortality during the study period as diagnosed by the clinicians in the three health facilities.

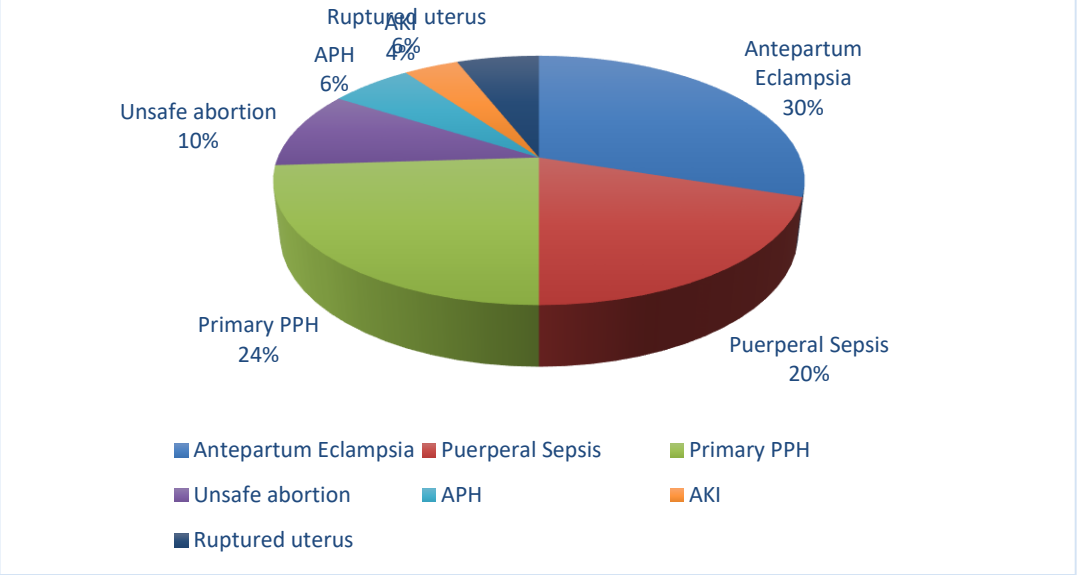
Table 6 9 Causes of maternal death (n=50 deaths)

Complication	Ilorin	Abuja	Bauchi	Total (%)
Obstetric haemorrhage	5	3	10	18 (36)
APH	1	0	2	3 (6)
PPH	3	3	6	12 (24)
Ruptured uterus	1	0	2	3 (6)
Antepartum eclampsia	6	0	9	15 (30)
Puerperal sepsis	4	0	6	10 (20)
Unsafe abortion	2	0	3	5 (10)
AKI	1	0	1	2 (4)
Total	18	3	29	50 (100)

PPH; post-partum haemorrhage APH; antepartum haemorrhage; AKI acute Kidney Injury

The most frequent groups of complications leading to maternal death were obstetric haemorrhage and hypertensive disorders (mainly eclampsia), which led to 36% (n=18) and 30% (n=15) of the maternal deaths respectively (**Table 6.9**; **Figure 6.7**). In terms of specific disease conditions, antepartum eclampsia was the most frequent cause of maternal death (n=15, 30%), followed closely by post-partum haemorrhage, which led to 12 deaths (24%). Puerperal sepsis was the next-commonest cause, accounting for a fifth (n=10, 20%) of all recorded deaths, and twice as many deaths as those that resulted from unsafe abortion (10%, n=5). The less common causes were antepartum haemorrhage, ruptured uterus and acute kidney injury, leading to three, three and two maternal deaths respectively (**Table 6.9**; **Figure 6.7**).

Figure 6 7 Causes of maternal death (n=50 deaths)



6.7.5. Analysis of outcomes

Maternal mortality and morbidity

Maternal mortality ratio was converted into number of deaths per 1000 live births for ease of analysis using chi-square testing. Comparing mortality in the baseline and the post-implementation periods, there was no significant change in the deaths in either the intervention or control arms of the study (**Table 6.10**).

There were no records of maternal near misses based on WHO near-miss criteria in any of the three study hospitals. Hence, maternal morbidity was defined as diagnosed by clinicians in the patients' medical records. Although the prevalence of morbidity varies significantly across the study arms, as presented earlier (**Section 5.3.4**), there was no change in prevalence within the trial arms following EWS implementation (**Table 6.10**).

Table 6 10 Prevalence of morbidity and mortality before and after EWS implementation

Intervention arm			
Condition	**Before (n=600)**	**After (n=600)**	**Chi-square P-value**
Maternal death/1000LB	1.32	1.46	0.432
Haemorrhage	10.7	11.1	0.313
Sepsis	12.2	12.7	0.226
Hypertensive disorders	10.5	9.8	0.081
Prolonged labour	10.3	10.4	0.174
Obstructed labour	9.8	9.8	0.261
Thromboembolism	0.3	0.2	N/A
Abortions	5.8	6.4	0.132
Control arm			
Condition	**Before (n=600)**	**After (n=600)**	**Chi-square P-value**
Maternal death/1000LB live births	1.36	1.28	0.115
Haemorrhage	5.2	4.9	0.112
Sepsis	8.8	8.7	0.354
Hypertensive disorders	7.5	7.6	0.881
Prolonged labour	7.7	8.0	0.326
Obstructed labour	1.3	1.8	0.099
Thromboembolism	0.0	0.0	N/A
Abortions	2.5	2.4	0.668

Length of hospital stay

Unlike in the control facilities, length of hospital stay in the intervention arm was significantly positively skewed (skewness: 2.33). The median (interquartile range) was therefore used in the outcome analysis. There was no significant change in the length of hospital stay following EWS implementation in the intervention hospital. Similarly, no change was observed in the control facilities (**Table 6.11**).

Table 6 11 Length of hospital stay (days) before and after EWS implementation

Variable	Baseline	After	t-test stat (p)
Intervention arm			
Median (IQR)	2 (1, 5)	2 (1, 4)	0.131
Control arm			
Hospital stay (SD)	2.4 (1.8)	2.3 (1.6)	0.117

ICU admission rate

Generally, the proportion of women admitted to ICUs across all study facilities was very low. Throughout the period of this study, only 14 (0.6%) were admitted to ICUs or high-dependency units due to direct obstetric complications. Analysing by study arm, there was no significant change in the ICU admission rate following EWS implementation in the intervention and the two control hospitals (**Table 6.12**).

Table 6 12 ICU admission before and after EWS implementation

Variable	Baseline	After	Chi-square P-value
Intervention arm			
ICU admission (%)	0.2	0.2	0.193
Control arm			
ICU admission (%)	0.7	0.4	0.066

Caesarean section (CS) and instrumental delivery rate

Caesarean section rate dropped significantly from 39.89% during the baseline period to 31.49% following implementation of the EWS in the intervention hospital. A significant rise was observed in the average CS rate of the two control hospitals (**Table 6.13**) in the post-implementation period. However, a sensitivity analysis showed a disproportionately higher caesarean birth rate in Abuja compared to Bauchi (61.4% and 22.1% respectively). Hence, a facility-level analysis was performed, which showed no significant change in the caesarean section rate in the

two control hospitals during the post-implementation period from the baseline rates.

Table 6 13 CS and Instrumental birth rate before and after EWS Implementation

Variable	Baseline	After	Chi-square P-value
Intervention arm			
CS rate (%)	39.89	31.49	0.002
Vacuum (%)	0.53	0.54	0.629
Forceps (%)	0	0	NA
Control arm			
CS rate (%)	31.41	36.49	0.004
Vacuum* (%)	0.54	1.22	0.103
Forceps* (%)	0.22	0.15	0.726

*Rate computed for only one (Bauchi) of the two control hospitals

As reported earlier (**Section 5.1.1**), overall instrumental delivery rate was very low in all three hospitals. Only four forceps deliveries were reported throughout, all conducted in Bauchi. No instrumental births were performed in Abuja, hence the estimate used in the outcome analysis was derived using data from Bauchi (**Table 6.13**). Considering the small number of instrumental births (few cells less than 5) (Altman & Royston, 2000), the appropriate test statistic for use was Fisher's exact test.

There was no significant change in the rate of vacuum deliveries following EWS implementation in the intervention hospital. Similarly, no significant change in the rate of instrumental deliveries (vacuum and forceps births) was observed in Bauchi (**Table 6.13**).

Frequency of monitoring

Frequency of clinical monitoring of patients was assessed using patient monitoring indices for the four routinely monitored vital signs (respiratory rate, temperature, pulse rate and blood pressure). The patient monitoring index (PMI) was defined as the ratio of the observed to the expected frequency of vital signs monitoring over a 24-hour period. The expected frequency was defined for each hospital using hospital-specific protocols. Across all 3 hospitals, the guidelines for frequency of monitoring obstetric patients using the vital signs chart is to monitor them every 6 hours (at least 4 times in 24 hours). While this applied for the intervention hospital during the baseline period, the expected frequency of monitoring during the post-implementation period was as specified by the EWS escalation protocol; i.e twice

daily for EWS scores of 0 or 1, 30-minutes apart for score of 2 and immediate referral for scores of 3 or more.

Table 6 14 Mean (SD) daily frequency of vital signs monitoring before and after EWS implementation

Intervention Hospital: Patient Monitoring Indices (PMI)			
	Baseline	**After**	**t-test (p)**
Temp (SD)	0.48 (0.38)	0.90 (0.38)	<0.005
Pulse (SD)	0.62 (0.33)	0.91 (0.38)	<0.005
RR (SD)	0.54 (0.37)	0.91 (0.38)	<0.005
BP (SD)	0.63 (0.33)	0.91 (0.37)	<0.005
Control Hospitals: Absolute monitoring frequencies			
	Baseline	**After**	**t-test (p)**
Temp (SD)	1.68 (0.89)	1.62 (0.88)	0.234
Pulse (SD)	1.75 (0.90)	1.66 (0.89)	0.123
RR (SD)	1.77 (1.25)	1.78 (1.24)	0.221
BP (SD)	1.77 (0.90)	1.70 (0.86)	0.115

A significant improvement in the frequency of monitoring all four vital signs was observed in the intervention hospital following EWS implementation (**Table 6.14**). This was especially so for temperature and respiratory rate monitoring, with baseline mean (SD) PMI of 0.48 (0.38) and 0.54 (0.37), and post-implementation mean (SD) PMI of 0.90 (0.38) and 0.91 (0.37) respectively. No significant change in the frequency of vital signs monitoring was observed in the two control hospitals (**Table 6.14**).

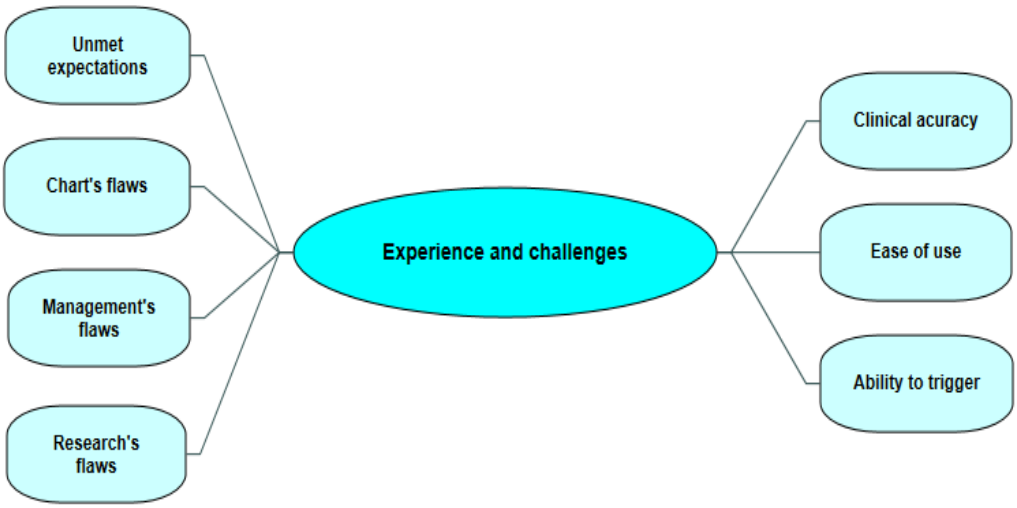
6.7.6. Experience and challenges of using EWS

Twelve key informant interviews and six focus group discussions were conducted with the clinical staff at the end of the study (April 2019) in the intervention site. Experience of using EWS and challenges encountered during the study period were explored among participants using open-ended interview questions and prompts. Interviewees consisted of seven senior nursing officers (five chief nursing officers heading the five wards: gynae emergency, antenatal, postnatal medical, postnatal surgical and gynaecology wards, and two assistant chief nursing officers) and five medical doctors (two senior registrars, two registrars and one intern in the Obstetrics and Gynaecology department). FGDs were conducted with nurses and midwives, each session having five participants from the participating wards.

Figure 6 8 Word frequency query (word cloud) of phase 3 interviews and FGD transcripts

The transcripts were first explored to gain a preliminary understanding of the concepts using NVivo word frequency queries (**Figure 6.8**). Vital signs, patients, midwives, doctors, challenges, introduced, and early warning were the most frequent words in the data, as illustrated in the word cloud (**Figure 6.8**). Exploring experience and challenges of using EWS in a thematic framework analysis, seven themes emerged, under which our findings are presented. These are clinical accuracy, ease of use, ability to trigger, unmet expectations, management's flaws, chart's flaws and research's flaws (**Figure 6.9**).

Figure 6 9 Visual map of themes relating to experience and challenges of using EWS



Clinical accuracy

Most of the nurses and midwives found the EWS chart useful in alerting them when to escalate care from doctors. They reported that abnormal observations are usually an indicator that the patient needs more frequent monitoring. In addition to contributing to the early detection of problems, the majority of the nurses/midwives felt that the chart assisted them directly in managing sick patients. These findings are illustrated by the following quotes:

> *"The chart has eased our work to a large extent, it alerts the nurses… I mean alerts us when to call the doctors in… (FGD Nurse)"*
> *"…it was accurate in that all patients with high scores are always the sick ones. In fact, it even assists us in monitoring how our post-operative patients are recovering after caesarean section… (KII Nurse)"*
> *"…The chart was quite useful in alerting us on when to call for help regarding a patient… this enhances early and timely intervention. So, will be very beneficial to both staff and patients… (FGD Nurse)"*

Similar to the nurses, the doctors felt that it was a good monitoring tool if properly followed. It was useful to have the "ability to follow a patient in time". They found the charts easy to correlate with a patient's clinical picture and reported that abnormal scores were usually consistent with clinical deterioration. Doctors also felt the chart could potentially help nurses to cope with the demands of their work (in view of gross shortage of human resource for health) while making it easier to detect unwell patients. These findings are illustrated by the following quotes:

> *"I have been called on few occasions to review patients based on the chart and to be honest, all the patients were truly ill (KII Doctor)"*
> *"It is very important for the patient and for us, as you know we have limited manpower (especially our nurses' colleagues), coupled with the number of patients that troop in daily, so if used properly, it can simplify the nurses' jobs helping them to prioritise the time to the real sick patients. (KII Doctor)"*

Ease of use

Compared to the routinely used vital signs chart, most of the nurses felt EWS was easier to use because of less frequent monitoring of clinically stable patients. By scoring vital signs and having a cumulative EWS score, the chart "compresses clinically relevant parameters into a simple score, making it easy to evaluate patients at a glance".

> *"… Clinical information of patients is compressed into a single score, making it easy to evaluate at a glance … (FGD nurse)"*
>
> *"… It was fantastic. The chart was easy to understand…, after we have filled vital signs, the scoring makes it easy to understand and compare the trends… (KII nurse)"*

Ability to trigger

Considering our finding of low rate of clinical review among triggered patients (38.9%), possible explanations were explored in interviews and FGDs. The postnatal surgical ward had the lowest trigger rate among all inpatient wards; however, patients admitted to the ward were at increased risk of trigger at baseline from caesarean section as mode of delivery (baseline EWS of 1 for stable patients). According to the ward nurses, this resulted in an initial high rate of false alarm from patients coming from the theatre. Often, the patients calm down (EWS score settles) with analgesia and rest. The EWS trigger threshold was therefore changed to 4, and the 30 minutes' review of sub-trigger scores was cancelled by the ward CNO.

Some FGD nurses reported doctors being inaccessible when needed to review triggered patients. These findings are illustrated by the following quotes:

> *"…repeating observations after 30 minutes is not feasible doctor. We receive up to four patients from the theatre daily… (FGD nurse)"*
>
> *"…Personally, I don't feel a patient coming from the theatre scoring 2 should be reviewed in 30 minutes. Moving her on the trolley alone can aggravate pain and raise blood pressure. From experience, they calm down with just analgesics and bed rest… (KII Nurse)"*

Unmet expectations

Although most staff felt the EWS was useful in patient monitoring and should be part of routine care, a few participants expressed dissatisfaction with the implementation. Specifically, they reported that their need for financial incentives as expected was unmet. Some typical quotes illustrating this are as follows:

> *"Like the pain score study, they gave us incentives, am sure if you had done the same the uptake wouldn't have been as poor… (KII Nurse)"*
>
> *"At the Liverpool training, we were given some stipends, I thought the source is the same… (FGD Nurse)"*

The chart's flaws

All doctors and most nurses felt a colour-coded EWS would have been easier to use and more efficient in picking out and communicating the need for clinical review than the black-and-white paper-based EWS chart. Additionally, it would be less labour-intensive and more visually appealing, hence more likely to be accepted by clinical staff. Therefore, they recommend that coloured EWS charts be implemented after the pilot study, given that the hospital management has already approved EWS implementation.

A few midwives found the instructions on the EWS escalation protocol ambiguous and believed this was a common cause of error in patient monitoring using EWS, especially among newly deployed (rotated) staff nurses.

The nurses on the ward opined that a space to record fetal heart rate should be added to the EWS chart, considering the importance of the parameter in assessing fetal well-being. These findings are illustrated by the following quotes:

> *"A coloured chart would be easier to use than this… am sure you chose black and white because of low production cost, but the management should adopt the coloured chart… (KII Doctor)"*
>
> *"I think coloured charts are abler to detect and communicate danger sign because anyone who sees red colour knows all is not well…KII Doctor"*
>
> *"…a major limitation of the chart in my opinion is absence of parameters that monitor the baby. I think a column on fetal heart rate should also be on the chart … (FGD N05)"*

Management's flaws

Major limiting factors to effective monitoring of vital signs using EWS that were identified were availability of functioning equipment and staff rotation by the hospital management. There was a gross shortage of patient monitoring equipment across all five wards. Although the hospital management has approved that EWS substitute routinely used vital signs chart for all obstetric inpatients, some nurses reported having to use the old monitoring chart concurrently with the EWS charts, which further stretched the already scarce patient monitoring equipment.

Rotation of staff, especially nurses/midwives (and medical interns), brings in new clinical staff who are untrained in the use of EWS. Rotation of nurses is usually conducted every six months by the department of nursing services. This happened shortly after the EWS implementation, taking most of the trained nurses to other clinical departments. This significantly affected the recruitment rate and overall success of the pilot study.

Another challenge related to hospital management that was reported by most doctors and nurses was gross shortages in human resources, especially of staff nurses and midwives. Afternoon shifts in some wards (mostly postnatal medical ward) are often covered by only one staff nurse.

The following quotes substantiate the above findings:

"Rotation happens every six months and new staff need to be trained for continuity… (KII Nurse)"

"In fact, shortly after you left, around mid-December was when the two of us were posted to ANC ward… (FGD Nurse)"

"…You know interns rotate, so are nurses, most of the errors in scoring are caused by lack of continuous training (KII Doctor)

"…we don't have enough staff, like in the postnatal medical ward, you find only one nurse covering most afternoon shifts… (KII nurse)"

"…like here we have only one BP machine on the ward, and to check patient's oxygen saturation you have to transfer her to gynae emergency ward… (FGD nurse)"

Research's flaws

The commonest emerging theme related to the limitations of this research was insufficient training of staff. All participants felt that the training at the beginning was inadequate and should have been ongoing throughout the post-implementation period and after the study. Nurses, midwives and interns in the maternity department need continual training on scoring, as illustrated by the quote below:

> *"Most common errors made were related to wrong scoring due to somewhat confusing EWS scoring guideline" (KII Nurse).*

Delayed supplies of the EWS chart by the research assistant were reported by some ward nurses. This had caused them to go back to using the old vital signs charts when EWS charts ran out. A few nurses also reported having to use the old chart concurrently with the EWS as the latter was always retrieved at the end of hospital stay for analysis. These findings are illustrated by the following quotes:

> *"…You know interns rotate, so are nurses, most of the errors in scoring are caused by lack of continuous training (KII Doctor)"*
> *"…You know interns rotate, so are nurses, most of the errors in scoring are caused by lack of continuous training (KII Doctor)"*
> *"The few of us that attended the training could not teach the new ones because of high workload and your colleagues come here only briefly… (FGD Nurse)"*
> *"Some of us taught ourselves this thing doctor, so you should commend, not criticize us for not scoring… (FGD nurse)"*
> *"… You, people, take the chart out at the end, so what evidence do we have to show that we have done the vitals? ... So we just use both charts (FGD nurse)"*

6.8. Chapter summary

Chapter 6: Implementation and evaluation of EWS

- The chapter presented the third phase of this PhD research, which aimed to implement and evaluate the use of obstetric EWS in a low-resource tertiary healthcare setting.
- A controlled quasi-experimental before–after trial was employed (one tertiary hospital in the intervention, two others in the control arms) to assess the effectiveness of EWS in improving health outcomes.
- Qualitative interviews (12 KIIs with doctors and senior nurses/midwives) and FGDs (six with junior nurses and midwives) were conducted to explore the experience and challenges of using the EWS.
- Baseline quantitative data were collected (1200 participants) for three months (August to October 2018) and post-implementation data (n=1200) were collected for four months (December 2018 to March 2019).
- Average recruitment rate was 78.1%, SBR was 64.6 per 1000 births, caesarean birth rate was 31.8% and estimated MMR was 1052 per 100,000 live births.
- Only half of the research participants (51.2%, n=307) in the intervention hospital had EWS scored; of these, 58.6% (n=180) required clinical review but only 38.9% (n=70) were reviewed by a doctor. Of the remaining half (48.3%, n=293), 48 (16.4%) patients would have required a review and were thus called missed opportunities.
- There was no significant change in the prevalence of maternal death, direct obstetric complications, ICU admission rate or length of hospital stay between the baseline and post-implementation periods across either study arm.

- The patient monitoring index (PMI; defined as the ratio of the observed to the expected frequency of vital signs monitoring over a 24-hour period), taken as a proxy for quality of vital signs monitoring, showed a significant improvement following EWS implementation in the intervention hospital. In the control hospitals, with similar baseline frequency of vital signs monitoring to that of the intervention hospital, no change in frequency was observed during the post-implementation period.
- There was a significant reduction in the caesarean birth rate (from 39.89% to 31.49%) following EWS implementation in the intervention, but not in any of the control hospitals. It was difficult to attribute this reduction to EWS implementation given that other quality improvement programmes (EmOC training: assisted vaginal delivery, caesarean section and perioperative care) took place concurrently with the EWS implementation.
- Clinical staff in the intervention hospital found EWS easy to use, easy to evaluate at a glance, capable of guiding referral and very accurate, with scores always correlating with the clinical picture of patients.
- Nurses and doctors felt the training provided was inadequate and stressed the need for training and retraining given that nurses and interns keep rotating in and out of the maternity units.
- Attitudes towards the EWS were positive in the majority of staff in the department, with the feeling that it helped staff to cope with the demands of their work while making it easier to detect and manage deteriorating patients.
- Identified limiting factors include shortage of human resource for health0, insufficient monitoring equipment, retrieval of the EWS chart for analysis (forcing some nurses to use both old and new charts), delayed stocking of EWS charts, and unmet expectations of financial incentives.

Chapter 7: Discussion, conclusion and recommendations

7.1. Overview of the chapter

*This chapter discusses the results of the third phase of the PhD project (**Chapter 6**: Implementation and evaluation of EWS), in relation to key findings of the previous phases, and the wider literature on EWS in obstetrics (presented in **Chapter 2**). These are presented according to the specific objectives of the thesis. The chapter then proceeds to discuss the strengths and limitations of the thesis, as these affect interpretation of the main findings, then draws key conclusions, underscoring their applicability to other, similar settings. Finally, the chapter itemizes the unique contributions of the PhD project to the body of knowledge, lays out specific recommendations and proposes a research agenda going forward.*

7.2. Background

We have established evidence, based on a systematic literature review, conducted as part of this PhD project, that EWS are effective in predicting severe obstetric morbidity and mortality, and hence can potentially contribute to improved quality of care, prevent progressive obstetric morbidity and improve health outcomes (Umar, A., et al*.,* 2019). The review (presented in **Chapter 2**) also showed that clinical parameters in most obstetric EWS versions are routinely collected in resource-limited settings, and therefore implementing EWS may be feasible in such settings. However, there was limited evidence on the effectiveness of EWS in reducing maternal deaths across all settings (Umar, A., et al*.,* 2019).

Going forward in the research, we conducted baseline formative research to assess the feasibility of implementing EWS in three Nigerian tertiary hospitals (findings presented in **Chapter 4**). Using a robust data set consisting of women with severe maternal outcome (maternal death or near miss) collected across 42 Nigerian tertiary hospitals (Oladapo et al*.,* 2015), we developed a statistically derived obstetric EWS model and score-based chart for use in low-resource settings using recommended model design methods (presented in **Chapter 5**) (Collins et al., 2015a; Umar A, 2019). This was implemented in a university teaching hospital in Nigeria, as part of the extended emergency obstetric care capacity-building programme (assisted vaginal delivery, caesarean section and perioperative care) by

the Centre for Maternal and Newborn Health, Liverpool School of Tropical Medicine. After implementation of the EWS, mixed research methods were used to assess its effectiveness in improving health outcomes and explore the experience of health workers/managers implementing the EWS (findings presented in **Chapter 6**).

In this chapter, the main findings of the research are summarized by the specific objectives. These are discussed in relation to the existing literature, giving more emphasis to the phase 3 findings, which were not discussed in the previous chapter. Then conclusions are drawn, key contributions of the research to the body of knowledge on maternal care monitoring are itemized, and specific recommendations are made for future research, policy and practice.

7.3. Feasibility of obstetric EWS implementation in low-resource settings

Monitoring was primarily performed by nurses and midwives across all study sites, whose scope of work was significantly hampered by gross shortages in human resources for health, and patient monitoring equipment (needed to monitor blood pressure, temperature, oxygen saturation). Similar challenges were reported following a recent feasibility assessment of MEOWS implementation in an Ethiopian tertiary referral hospital (Moore et al*.,* 2019), but not in India (Singh, S., et al*.,* 2016) or Zimbabwe (Merriel et al., 2017).

During the feasibility study, we found that pulse, respiratory rate, blood pressure and temperature were recorded at least once in every clinical shift in spite of existing challenges (**Chapter 4**). In addition to patient consciousness level, which can be evaluated without any monitoring equipment, the four parameters were the most frequently used EWS parameters, included in 14 of the 16 reported obstetric EWS charts included in our systematic review (Umar, A., et al*.,* 2019). Measuring these parameters requires simple patient monitoring devices that are readily accessible (BP machine, a thermometer, and a clock/watch or timer). This finding suggests that it may be feasible to implement EWS in settings where more sophisticated patient monitoring and diagnostic equipment may be unavailable.

None of the three hospitals included in the feasibility study uses a bleep or paging system for communication. It was, however, shown that effective escalation of care happened within and between nurses/midwives and doctors via verbal messages, sending of hospital assistants or phone calls, and occasionally through dispatch of call duty vehicles (**Chapter 4**). This is similar to the practice in the phase 3 intervention hospital, and comparable to the existing trigger system following EWS implementation in similar settings in Zimbabwe and Ethiopia (Merriel et al., 2017; Moore et al., 2019).

Although a lot of work has taken place in many countries outside the UK to assess the benefits of obstetric EWS, only a few studies have researched the feasibility of implementing EWS and their usefulness in low-resource settings. Merriel and colleagues (Merriel et al., 2017) implemented a modified obstetric early warning system in a government referral hospital in Bulawayo, Zimbabwe. The aim of the before–after study was to develop and implement a locally applicable modified obstetric EWS to determine whether patients can be better stabilized before transfer to theatre, and whether more timely action can be taken when patients begin to deteriorate. Studying women undergoing caesarean section before (n=79) and after (n=84) implementation, the study reported a significant improvement in preoperative stabilization (odds ratio 2.78, 95% CI 1.39–5.44) and improvement in action taken due to abnormal findings (Merriel et al., 2017).

The study reported successful EWS implementation, identifying a need to scale it up to ensure replicable findings. However, major limitations were identified with the overall conduct of the research (Merriel et al., 2017). First, parameter selection for the chart was based on subjective assessment, not a conventional model design and validation process. Next, the parameter values selected as cut-offs were not evidence-based. However, these challenges are not peculiar to the study as they were also reported for several other obstetric EWS versions (Singh et al., 2012; Smith et al., 2017; Umar, A., et al*.,* 2019). Finally, owing to limited resources, the chart was applied to a selected group of patients (Merriel et al., 2017). This could possibly limit the potential of the EWS to be a safety net to identify those “normal” women who begin to develop complications.

More recently, Moore and colleagues introduced a colour-coded modified obstetric EWS (MOEWS) for parturients who had undergone surgical interventions in a tertiary referral hospital in Ethiopia (Moore et al., 2019). Felege Hiwot Referral Hospital (FHRH) is one of 82 referral hospitals across the whole of Ethiopia and serves a population of seven million people. FHRH has a delivery rate of almost 6000 per year and a caesarean section rate of 35%–40%, equating to between 2000 and 2400 caesarean sections per year (Merriel et al., 2017). The facility-based MMR rate has been between 300 and 400 per 100,000 for the past three years (FHRH Obstetrics department & FHRH management, personal communication, 2019).

The chart was specifically developed for the local setting (Moore et al., 2019). A guideline was developed to accompany and guide EWS trigger management, together with training of healthcare workers. However, as in the report of Merriel and colleagues, trigger cut-off selection was not evidence-based, as this was determined by a joint discussion of obstetricians, anaesthetists and the local hospital management (Merriel et al., 2017). Similarly, parameter selection for the chart was based on consensus, not a conventional model design and validation process (Collins et al., 2015), and hence it has a weak evidence base. Prior to EWS introduction, the quality of post-operative monitoring was assessed through retrospective case note reviews. This was reassessed at eight months and 11 months post implementation, with assessment of response to triggers. A mixed-method research approach was used to establish views of healthcare workers on feasibility of implementation, acceptability and usability. The study reported that the EWS is a feasible and acceptable tool for coping with the unique demands faced in low-resource settings, provided modifications are made to suit the setting and senior clinician involvement, coupled with regular training of clinical staff, is ensured.

Overall, healthcare service delivery in low-resource settings can be tasking. Commonly reported challenges were increased workload from inadequate staff capacity, insufficient or inefficient equipment available for patient monitoring, and lack of medical consumables (phase 1). Despite these challenges, however, the common physiological parameters in most EWS were monitored in our study

hospitals and other, similar low-resource settings (Merriel et al*.,* 2017; Moore et al., 2019; Paternina-Caicedo et al*.,* 2017; Singh, A., et al*.,* 2016; Umar, A., et al*.,* 2019). We also established the existence of a functional trigger mechanism across all study facilities. This, therefore, implies that implementing EWS in these settings is not only feasible but will potentially enable healthcare staff to cope with the demands of their work while making it easier to detect unwell patients.

7.4. Obstetric EWS chart for use in low-resource settings

Development and validation of a simple obstetric diagnostic prediction model and EWS for use in resource-limited settings was presented and discussed previously (in **Chapter 4**). Briefly, measurements of temperature, pulse rate, systolic blood pressure, respiratory rate and mode of birth in post-partum patients (caesarean section versus spontaneous vaginal birth) were the primary early warning parameters from the three statistical models for severe maternal outcome (SMO). Level of consciousness and urine output assessment were dropped from the statistical models due to perfect prediction of outcome, not statistical insignificance, hence were forced into the seven-parameter score-based EWS chart (**Annex 5A**). Scoring guidelines and escalation protocol were defined based on the MEOWS recommended in the reports of the 2005 CEMACH (CEMACH, 2007). To the best of our knowledge, this analysis reports for the first time the development and validation of a diagnostic prediction model and EWS for a general obstetric population in a low-resource setting based on recommended methodology (Collins et al., 2015a) using local data.

Following the serial validation, the chart's parameters showed an excellent predictive ability to discriminate women who developed severe maternal outcome from those who did not (area under ROC curves consistently above 90%). The model attained similar diagnostic predictive accuracy to that of one developed, internally validated (Carle et al*.,* 2013) and externally validated (Paternina-Caicedo et al., 2017) using data from obstetric intensive care unit patients. Our model also performed similarly to non-obstetric cardiovascular adult critical care and neonatal critical care score systems developed (Knaus et al*.,* 1981; Knuiman & Vu, 1997; Richardson et al*.,* 2001). Compared to other routinely used EWS in obstetric ward settings, our model has significantly better screening characteristics (positive

predictive value of 94%, 95% CI 93–95), compared to an average of 41% reported for 16 different EWS versions. (Umar, A., et al*.,* 2019) This is of particular significance, since an early warning system that generates many false positive findings may possibly worsen clinical care, and constitute a nuisance alarm by creating an excessive burden on the health system (Friedman et al*.,* 2015; Goldhill et al*.,* 2005).

Another peculiar strength of the EWS chart we developed is that measuring the seven parameters requires simple patient monitoring devices that are readily accessible (BP machine, a thermometer, and a clock/watch or timer). Compare this to parameters in the only other statistical EWS reported to date (Carle et al*.,* 2013): computing the fraction of inspired oxygen required to maintain SPO2 above 96%, this being one of the EWS parameters in this chart, could be quite challenging in low-resource settings, as arterial blood gases measurement, or even pulse oximetry measurement equipment, may not be readily available (Allegranzi, B., 2015) (also results of **Chapter 4**: Feasibility study). This makes our EWS chart friendlier to low-resource settings without compromising its efficiency.

7.5. Usefulness of EWS in improving outcomes

7.5.1. Reduction of maternal death

The average estimated institutional maternal mortality ratio across the phase 3 study sites was 1052 per 100,000 live births. This is significantly higher than the Nigerian national average of 814 per 100,000 live births (World Bank, 2015), but comparable to a hospital-based estimate of 1088 per 100,000 (Oladapo et al*.,* 2015). Leading causes of maternal death were pre-eclampsia/eclampsia (36%, n=18), obstetric haemorrhage (30%, n=15) and sepsis (20%, n=10). In a large country-wide hospital-based survey of 42 Nigerian tertiary hospitals, haemorrhage and hypertensive disorders were the most common causes of severe maternal outcome, accounting for 39% and 24% of SMOs, and 24.4% and 29% of maternal deaths respectively (Oladapo et al*.,* 2015). These are comparable to a global estimate from a WHO systematic review of global causes of maternal death where haemorrhage accounted for 27.1% (661,000, 19.1%–36.2%), hypertensive disorders 14.0% (343,000, 11.1%–17.4%), and sepsis 10.7% (261,000, 5.1%–18.6%) of maternal deaths around the world (Say et al., 2014b).

Comparing maternal mortality ratio in the baseline and post-implementation periods of the phase 3 research, it can be seen that there was no significant change in the intervention hospital (1.46 from 1.32 per 1000 live births, p-value 0.432), suggesting no effect of the intervention on the outcome. EWS had proved to be highly accurate in predicting maternal death, especially among critically ill obstetric patients (Carle et al*.,* 2013; Paternina-Caicedo et al*.,* 2017). However, our findings are not surprising given the systematic review report of limited evidence on the effectiveness of obstetric EWS in reducing maternal death (Umar, A., et al*.,* 2019).

Evidence has been established that delays in recognition, diagnosis and treatment precede the majority of maternal deaths from obstetric haemorrhage, hypertension, infection and venous thrombosis (Mhyre et al*.,* 2014; Saucedo et al*.,* 2013). Maternal mortality reviews indicate that a significant proportion of women who die due to pregnancy and childbirth demonstrate abnormal vital signs long before death, suggesting that a multi-parameter EWS system should identify them with high specificity (Mhyre et al., 2014b). Effectively, this should facilitate timely diagnosis and treatment, limit the severity of morbidity, and possibly reduce mortality. Maternal mortality is an extremely rare outcome; hence, a very large sample size is required to have a substantial number for effective analysis. Given that the implementation of EWS in this study involved a single facility with only 18 maternal deaths over the seven-month period of the research, large multicentre randomized controlled trials will be required to evaluate the effectiveness of obstetric EWS in reducing death.

7.5.2. Reduction of morbidity and ICU admission

There were no records of maternal near misses based on WHO near-miss criteria in any of the hospitals included in this research. Hence, maternal morbidity was defined as diagnosed by clinicians in the patients' medical records. Following implementation of obstetric EWS in the intervention hospital, there was no significant reduction in the prevalence of obstetric haemorrhage, hypertensive disorders, sepsis, prolonged labour, obstructed labour, thromboembolism or abortions. No change in prevalence of these conditions was recorded in the two control hospitals either. This suggests no effect of the EWS intervention on the outcomes. Similarly, we observed no significant change in the rate of obstetric

admissions to intensive care and high-dependency units following EWS implementation.

EWS has been shown to prevent progressive obstetric morbidity (Shields et al*.,* 2016; Hedriana et al*.,* 2016; Umar, A., et al*.,* 2019). In contrast to our findings also, Shields and colleagues, in a large multicentre quasi-experimental trial, reported a significant reduction in severe and composite maternal morbidity ($p<0.01$) as defined by the Centre for Disease Control (CDC), but not mortality, in six intervention hospitals following EWS implementation, compared to 19 control hospitals (Shields et al*.,* 2016). However, they also observed no change in the ICU admission rate in either the intervention or control hospitals (Shields et al*.,* 2016).

Although we did not find any change in the proportion of direct obstetric complications, we are aware that clinical outcomes would only have been improved (prevalence of morbidity and mortality reduced) if completion of the EWS had led to escalation of intervention, physician assessment as specified by the system, and institution of appropriate interventions. It could be argued that the period post implementation (four months) would not have been sufficient to allow such changes to manifest, especially considering the designs of similar studies that measured outcomes after longer periods (12–18 months) (Merriel et al*.,* 2017; Moore et al., 2019; Shields et al*.,* 2016). It could also be argued that the lack of standardization of morbidity outcomes used in our analysis limits its comparability to findings of similar studies. The latter limitation is, however, not specific to our research, as previously reported in EWS validation studies (Singh, A., et al*.,* 2016; Singh, S., et al*.,* 2012; Umar, A., et al*.,* 2019).

7.5.3. Caesarean section (CS) rate

Overall, caesarean births constituted 25.2% and 31.8% of all births in the feasibility and phase 3 study hospitals respectively. These estimates are clearly in excess of the proportion of 10%–15% of births that is thought to be optimal at population level (Betran et al*.,* 2015; Boerma et al*.,* 2018; Vela et al*.,* 2014; World Health Organization, 2015), and a significant increase from a 2009 report of hospital-level CS rate of 14% in Nigerian tertiary hospitals (Shah et al., 2009).

It has been widely cited in the literature that the World Health Organization (WHO) expert panel suggested in 1985 that "*There is no justification for any region to have caesarean section rates higher than 10–15 percent (World Health Organization, 1985)*". Following this, in the last three decades the caesarean section rate has continued to increase in an unprecedented manner in both developed and developing countries (Boerma et al*.,* 2018; World Health Organization, 2015). On the basis of data from 169 countries that include 98.4% of the world's births, a recent global estimate reported that 29.7 million (21.1%) births occurred through CS in 2015, which was almost double the number of births by this method in 2000 (16.0 million, 12.1%) (Boerma et al., 2018). This rise has been shown to be driven by major increases in non-medically indicated CS in many middle-income and high-income countries (Betran et al., 2015; Vela et al., 2014). When medically justified, a caesarean section can effectively prevent maternal and perinatal mortality and morbidity; however, there is no evidence showing the benefits of caesarean delivery for women or infants who do not require the procedure (World Health Organization, 2015c).

In a recent systematic review of ecological studies, Betran and colleagues reported a strong inverse relationship between CS rates and mortality outcomes such that maternal, neonatal and infant mortality decrease as CS rate increases up to a certain threshold (9%–16%); above this threshold, caesarean births were not associated with decreases in mortality outcomes after adjusting for confounders (Betran et al., 2015).

Following implementation of EWS during phase 3 of this project, the CS rate dropped significantly in the intervention hospital (from 39.89% to 31.41%, chi-square significance (p) = 0.002), but not in any of the control facilities. It was difficult to attribute the reduction to EWS implementation as this was a component of the extended EmOC capacity-building programme that was implemented at the same time (EmOC training: assisted vaginal delivery, caesarean section and perioperative care). No other quality improvement project happened concurrently during the 4-month post implementation period, but one of the key topics of the EmOC programme was interventions to reduce unnecessary caesarean sections. However,

individual-level analysis of indications for caesarean births during the baseline and post-implementation periods was not performed due to resource and logistic constraints.

7.5.4. Instrumental vaginal delivery rate

Prolonged and obstructed labour are important causes of maternal morbidity and mortality, particularly in low-income countries (Hofmeyr, 2004; Say et al*.,* 2014). Complications of prolonged and obstructed labour cause 4%–13% of maternal deaths in Africa, Asia, Latin America and the Caribbean (Ameh, C., et al*.,* 2009; Say et al*.,* 2014). In our phase 3 study cohorts, obstructed labour complicated approximately 10% of pregnancies in the intervention and 5% of pregnancies in the control health facilities. Current obstetric practice employs instrumental vaginal delivery techniques using obstetric forceps or vacuum extractor to achieve the best possible outcomes in cases of poor labour progress, maternal exhaustion, presumed fetal jeopardy, medical conditions that require shortening of the second stage of labour, and other common clinical problems (Green-top Guideline, 2017). These are evidence-based interventions that have been proved to be effective and are provided in both basic and comprehensive essential (or emergency) obstetric care health facilities, the WHO handbook on EmOC (2009), and new EmOC signal functions (Ameh, C., 2009; Gabrysch et al., 2012; Maine, D., et al*.,* 1997).

The overall instrumental delivery rate was very low in all phase 3 study hospitals. Only four forceps deliveries were reported throughout, all conducted in one control facility (Bauchi). No instrumental vaginal births were performed in the second control facility (Abuja). In the intervention hospital, only seven vacuum deliveries were conducted over the seven-month period, three before and four after the EWS implementation. Using the Fischer's exact test, the difference in the two rates was not statistically significant (0.53 to 0.54, p=0.629), suggesting that obstetric EWS implementation did not have an effect on the practice of instrumental vaginal births.

The extremely low use of forceps and ventouse is, however, not peculiar to our study settings. Generally, there has been a decline in operative vaginal delivery worldwide (Okeke & Ekwuazi, 2013). Reported rates vary greatly between settings

and the ideal rate is unknown (Ameh, C., et al*.,* 2009). In developed countries, the instrumental vaginal delivery rates vary from 10%–13% in the UK (Green-top Guideline, 2011) to 4.3% in the USA where its rate has halved in the last 20 years (Dildy et al*.,* 2016); additionally, the precipitous decline in both resident training in the use of obstetric forceps and forceps deliveries in the USA has been said to share striking similarities to observations regarding the decline and ultimate extinction of biological species (Dildy et al., 2016).

Significantly lower rates of instrumental vaginal births (<1%) were reported for other low-resource settings, which was linked to higher mean parity of patients, unavailability of epidural analgesia and electronic intrapartum fetal monitoring (Ameh, C., 2009; Bailey, 2005; Shah et al., 2009). With the rate of caesarean section known to vary inversely as the rate of instrumental delivery (Dildy et al., 2016), a high CS rate could have played a key role in the observed low uptake in our study cohort. Furthermore, despite the assisted vaginal delivery training provided, there may be other factors that influenced the practice of assisted vaginal delivery that were not investigated as part of this PhD. Nevertheless, the implications of low uptake of forceps and vacuum deliveries are outside the scope of this thesis.

7.5.5. Frequency of patient monitoring

Following implementation of the EWS chart in our phase 3 intervention hospital, all study participants (n=600) had their monitoring charts retrieved at the end of hospital stay for analysis. Overall, recording of EWS parameters was incomplete, with regular monitoring (at least two times in 24 hours) of temperature, pulse, respiratory rate and blood pressure performed in just over half (54%) of the study participants. The least frequently monitored EWS parameter was delivery mode for post-partum patients, which was recorded at least once daily in just over half (55%), and regularly in only about a third (29.8%), of the study participants. Unlike the other EWS parameters, mode of birth does not change over time. We therefore acknowledge that health workers may not have seen the need to repeat the information on the EWS chart according to the escalation protocol. However, mode of birth has been shown to significantly affect the risk of SMO, with women who had CS having a risk of developing SMO at least five times higher than those who had SVD (three SMO models in **Chapter 5**). Given this, strong effort is necessary to

persuade clinical staff to view recording of the parameter as a means to prevent SMO, and not just a repetition of unchanging information.

Moreover, even when parameters were measured and recorded on the EWS charts, only 15.4% (n=92) of the study participants had EWS scores documented according to the phase 3 study protocol (at least twice in 24 hours). Other studies also reported incomplete monitoring of clinical parameters in obstetric EWS (Merriel et al., 2017; Moore et al., 2019; Sheikh et al., 2017), including where EWS was implemented in well-resourced settings (particularly low recording of respiratory rate) (Edwards et al., 2015; Lappen et al., 2010; Maguire et al., 2015).

The patient monitoring index was taken as a proxy for quality of vital signs monitoring (respiratory rate, temperature, pulse rate and blood pressure), as in previous studies (Maguire et al., 2015; Merriel et al., 2017). The patient monitoring index was defined as the ratio of the observed to the expected frequency of vital signs monitoring over a 24-hour period. By monitoring stable patients after every 12 hours based on the EWS escalation protocol in the intervention hospital during the post-implementation period, staff undertaking monitoring are allowed to prioritize allocating their time to clinically unstable patients. The patient monitoring index showed a significant improvement following EWS implementation in the intervention hospital. This was especially so for temperature and respiratory rate monitoring, with mean (SD) PMI of 0.48 (0.38) and 0.54 (0.37) in the intervention hospital at baseline, increasing to 0.90 (0.38) and 0.91 (0.37) respectively post implementation. With a similar baseline frequency of vital signs monitoring as the intervention hospital, no change in frequency was observed in the control hospitals during the post-implementation period (**Chapter 6**, **Section 5.6.5**). This is consistent with findings of one before–after study (before n = 61, after n = 20), which reported an increase in the frequency of documentation of vital signs following implementation of the Irish Maternity EWS on obstetric patients with sepsis (P. J. Maguire, O'Higgins et al., 2015). Our findings also support the report that introduction of modified obstetric EWS improves the post-operative monitoring of women after caesarean section (Merriel et al., 2017; Moore et al., 2019; Sheikh et al., 2017).

7.5.6. Experience of using EWS

Clinical staff in the phase 3 intervention hospital reported finding obstetric EWS easy to use. Design of the chart (with provision for cumulative EWS scores) made it easy to evaluate at a glance and easy to track changes in patient's clinical conditions over time. These findings are consistent with some reported experience following EWS implementation in similar settings (Merriel et al., 2017; Moore et al., 2019), and in well-resourced settings (Shields, 2016; Singh, S., et al., 2012). Similar findings were also reported following implementation of EWS in Mbarara University Hospital in Uganda (Walker, 2012). In this hospital, lay healthcare workers used a "lay MEWS" to monitor patients; this allowed them to involve nursing staff when the condition of the patient reached the trigger threshold based on an escalation protocol. This proved an efficient way to deal with the nursing staff shortage in that hospital.

The nurses reported that EWS was capable of guiding their judgement on patient referral, and clinicians found it accurate, with scores always correlating with the clinical picture of patients. They also reported good staff attitude towards EWS, with the feeling that it helped them to cope with the demands of their work while making it easier to detect and manage deteriorating patients. These reports are hard to correlate with our observed low usage rate of EWS in phase 3, where only half of the study participants (51.2%, n=307) had EWS scores recorded at least once in 24 hours, and just 15.4% (n=92) had EWS scores documented as prescribed by the study protocol (at least twice in 24 hours).

Given that the interviews and FGD sessions were all convened by the principal researcher and two members of the local implementation team, all of whom are doctors, we acknowledge the possibility of having normative responses from participants, despite attempts to be non-judgemental. The feasibility study reported poor understanding of potential usefulness of vital signs as early warning pointers of maternal deterioration among nurses and midwives (Chapter 4: Feasibility study). This might not have been addressed despite staff training prior to EWS implementation in phase 3, hence could have played a role in the observed low usage rate. Having said this however, similar inconsistencies have been

reported about the use of partograph previously; assessing knowledge and utilization of the partograph among midwives in two tertiary health facilities in the Niger Delta Region of Nigeria, Opiah and colleagues (2012) reported a wide disparity in nurses' account and the observed completion rate. Although 98.8% of the nurses and midwives reported routine use of the partograph in the two hospitals, assessment of utilized partograph charts revealed that only 18 (37.5%) out of 48 in one hospital, and 17 (32.6%) out of 52 in the other hospital were properly filled (Opiah et al, 2012). Comparatively, poor usage rate of partograph (average of 21.8%) has been widely reported in other settings (Mabasa S.K.M, 2018).

7.5.7. Implementation challenges and solutions

As projected during the feasibility study, human resource shortages and insufficient monitoring equipment were common limiting factors in recording of vital signs and effective patient monitoring using EWS in the phase 3 intervention hospital. Confounding this, some nursing staff in our phase 3 intervention hospital recourse to using two monitoring charts (EWS and old vital signs chart) despite a new policy by the hospital management to use the EWS only. This further stretched the already scarce patient monitoring equipment and human resources for health (more time spent completing charts).While these are common challenges in low-resource settings (Allegranzi & Pittet, 2007; Moore et al., 2019), addressing human resource and equipment shortages is likely not only to ensure successful EWS implementation, but also to help in solving the big problem of providing quality and timely health services to those in need (Aithal, A 2017)

Human resource shortage is a global health crisis, that is expressed in acute shortages and misdistribution of health workers, geographically and professionally (Bandiwala et al, 2010). This massive global shortage, though imprecise quantitatively, is estimated at more than 4 million workers, and is especially more pronounced in low income settings (WHO Global health workforce statistics, 2018).

Human resource for health challenges continue to constrain delivery of services in Africa. To respond to this crisis, policies and actions are needed to address the dynamics of the health labour market, the production and management of the

health workforce, and to strengthen the performance of existing health systems (WHO, 2018). The global strategy on human resource for health: workforce (2030) calls for affected countries to strive to use their own human resource for health to meet their needs, to collaborate towards more ethical and fair international recruitment practices, and to respect the rights of migrant health workers. Of more relevance to this thesis is the policy's emphasis on measures to improve pre-service training and skills building (WHO 2016: Global strategy on human resource for health: workforce 2030). Most of our study participants opined that the training provided on EWS use was grossly inadequate and stressed the need for continual training to ensure adherence.

In addition to closing the skills gap of maternity staff on EWS use, continuous training can potentially mitigate another challenge encountered following EWS implementation in our phase 3 intervention hospital. Rotation of clinical staff (especially nurses) across different hospital departments and wards was a major challenge to effective implementation of EWS in the EWS intervention site. The observed low recruitment rate (average of 78.8%), EWS completion rate (58.6%) and doctor's review rate (38.9%) for triggered patients were strongly attributed to rotation of untrained nurses into the Obstetrics and Gynaecology department, which happened two months after the EWS implementation (in December 2018). Hence, modification of staff deployment/rotation practices to ensure mandatory induction of newly deployed staff into the maternity units, that includes training on use of the EWS is necessary. While this may likely help to cope with high turnover of clinical staff (nurses, midwives and interns) in the short term, it may be argued that this is potentially unsustainable, as staff are likely to lose the acquired skill once deployed out of the obstetric units (Aithal A, 2017).

Although brief training sessions have proven effective in short- term improvement in objective measures of knowledge and comfort level in managing obstetrical events, the most important determinant of long-term retention, the available evidence suggests, is formal and prolonged contact with the domain, as obtains in curriculum based learning (Custers et al, 2010; Vadnais, et al 2012). Integrating EWS training into the curriculum of the schools of nursing and midwifery has been

suggested as a long-lasting and sustainable solution to the problem of high staff turnover. Additionally, this approach is likely to enhance understanding of potential usefulness of EWS vital signs as early warning pointers to maternal deterioration, which was found to be a challenge in our feasibility study (chapter 4). Similar recommendations were made following a pilot implementation of obstetric EWS in tertiary referral hospitals in Zimbabwe and Ethiopia (Merriel et al., 2017; Moore et al., 2019).

7.6. Study strengths and limitations

Details of ethical considerations and quality control measures specific to each research phase have been discussed previously (chapters 3, 4, 5 and 6). Below are what we considered the key strengths and limitations of this PhD project.

7.6.1. Strengths

The study was designed after evidence on the usefulness of obstetric EWS was established through an up-to-date systematic literature review (Umar, A., et al., 2019). To the best of our knowledge, this was the first systematic review to report predictive accuracy, and effectiveness of obstetric EWS in improving clinical outcomes. Other strengths of the review include adherence to the good practices of protocol registration and use of a robust tool for quality assessment in diagnostic accuracy studies.

The use of both qualitative and quantitative methods in the feasibility study allowed robust understanding of the patient monitoring practices in the facilities studied. The cross-sectional component used objective, routinely collected health facility data, thus minimizing the risk of information bias. For the qualitative component, trustworthiness was checked through triangulation of data from key informant interviews with focus group discussions. Findings from non-participant observations were corroborated with quantitative data from a review of secondary records to adjust for possible Hawthorne effect.

The main strength of the second phase of this study, and perhaps one of the major strengths of this thesis, lies in the robust maternal death and near-miss case data set used in the development and internal validation of the EWS model. These were prospectively collected data, primarily collected for research purposes, with very

few missing data (2.7% of participants). To our knowledge, this analysis reports for the first time the development and validation of a diagnostic prediction model and EWS for a general obstetric population in a low-resource setting with strict adherence to diagnostic predictive model development methodology as recommended by the TRIPOD statement (Collins et al., 2015a). Additionally, a common limitation of EWS validation studies was addressed in the phase 2 analysis. This is the lack of standardization of outcome measures, which is especially common with studies using morbidity as an outcome measure (including the third phase of this project) as, often, morbidity has been defined based on consensus or the opinion of clinicians rather than standardized definitions.

With the before–after study design, seasonal variations in obstetric complications can potentially affect the prevalence of primary outcome measures. Seasonal variations in utilization of healthcare facilities, possibly due to reduced access (adverse weather conditions affecting road transport), delayed or non-payment of salaries to workers, industrial action among healthcare workers (resident doctors', nurses' and allied health workers' strikes, which were quite common prior to this project in Nigeria) may affect the occurrence of other outcome measures. While it is acknowledged that these could still happen in a controlled quasi-experimental before–after study, fortunately these challenges did not affect any of the three facilities in either the before or after phase.

Although enormous implementation challenges were encountered, the hospital management has been quite supportive towards this research. Through the approval of EWS being substituted for routine vital signs charts and the dispatching of internal circulars to that effect across all obstetric wards, the major institutional barriers to implementation were broken. Additionally, the fact that the implementation was led by the local implementation team under the supervision of the local co-PI, who is a senior professor in the Obstetrics and Gynaecology department, eased access of the research team to key stakeholders in the intervention hospital.

Finally, the principal researcher was independent and not a staff member of any of the hospitals involved in this PhD project. As such, the researcher was neither

known nor connected to the different study sites. This allowed the study participants (interviewees and FGD participants) to be more open and not withhold information due to any concerns of compromising their job or care, as may be relevant.

7.6.2. Limitations

All health facilities included in this PhD research were tertiary hospitals that provided CEmOC services. Also, considering the scope and budget of this study, it was only feasible to implement the EWS in one hospital. This was, however, a large university teaching hospital and the only government tertiary healthcare facility servicing the entire Kwara state, with a population of 2.37 million (National Bureau of Statistics, 2018). If it is possible to implement the EWS chart in a busy hospital such as this, then it could be possible to implement it in other units where there are dedicated nursing/midwifery staff and a high turnover of obstetric patients. Owing to our constraints, however, the feasibility and utility of implementing the EWS chart in smaller centres (including primary healthcare facilities) with weak staff strength was not investigated in the present study. To improve generalisability of findings, further external validation should aim at different level of care including both primary and secondary centres.

The inclusion of parameters in our EWS chart was guided by well-established statistical methods of model design and validation. The regular measurement of a woman's vital signs is a universal feature of EWS and choosing the correct normal ranges for measured variables is fundamental to their appropriate, safe and efficient use. It suffices to say here that specific triggers used in the score-based EWS chart that was implemented in our phase 3 intervention hospital were derived from UK MEOWS, which was developed based on limited clinical and scientific evidence (CEMACH, 2007). Although it is known that pregnancy alters maternal physiology, data are lacking regarding the normal maternal vital signs ranges for each stage of pregnancy, labour and the post-partum period. Specific cut-off points to these stages may therefore evolve as future evidence develops.

With the before–after design, it is likely that the impact of the EWS implementation on health outcomes will be stronger soon after the intervention has been

implemented and that this will reduce with time. This is because there is a possibility that staff (nurses, midwives and interns) trained in each ward will not be retained within the Obstetrics department, mainly due to staff rotation. Once a critical mass of trained staff is lost from the research wards, it is likely that the quality of care will reduce. Although we employed surveillance and continuous training/retraining of clinical staff by the local implementation team, this remained a major limitation that significantly affected participants' recruitment to, and overall conduct of, phase 3 of this research.

We used a retrospective case notes review to establish a pre-implementation baseline in phase 3 of this project. However, there is evidence suggesting that nurses' documentation, or lack of it, may not reflect actual clinical practice, and hence this is a potential limitation (Jefferies, 2010; Moore et al., 2019). Additionally, while use of PMI to evaluate frequency of monitoring paid emphasis on the expected frequencies based on the hospital's and EWS escalation protocol during the two periods, we do acknowledge its potential to amplify effect estimates as a potential study limitation.

Individual-level analysis of indications for caesarean births during the baseline and post-implementation periods was not performed due to resource and logistic constraints. It was therefore difficult to attribute the observed decrease in caesarean section rate to reduction in medically unnecessary CS or EWS implementation. This was especially so given that other quality improvement programmes (EmOC training: assisted vaginal delivery, caesarean section and perioperative care) took place in the intervention facility concurrently with the EWS implementation.

Finally, despite medicine being practised in the English language across all study sites, responses to interviews and FGDs could have been limited by the respondents' ability to convey themselves in a second language.

7.7. Conclusion

Reducing maternal morbidity and mortality is a significant challenge worldwide. This is especially so in low-resource countries like Nigeria. One basic way to prevent

maternal deaths in healthcare facilities is through early detection of changes in physiological parameters that are suggestive of deterioration in clinical condition before such changes become irreversible and fatal. This is the aim of the obstetric EWS. The aim of this PhD project was to introduce and evaluate the use of obstetric EWS in Nigerian tertiary hospitals. To achieve this aim, a preliminary investigation of the evidence supporting the usefulness of EWS in obstetric practice was achieved via a systematic literature review. Findings from this review helped shape the structure of the project into three phases: a baseline feasibility assessment (phase 1), design/internal validation of obstetric EWS for use in low-resource settings (phase 2), and implementation and evaluation of the designed obstetric EWS in a Nigerian tertiary hospital (phase 3).

Key findings from the feasibility study showed a high burden of maternal morbidity and mortality, and confirmed absence of an early warning chart, a checklist or any guidelines on how to trigger responses to obstetric emergencies. Although vital signs were routinely monitored in the hospitals, understanding of their potential utility as early warning pointers to maternal deterioration was deficient among healthcare workers, especially nurses and midwives, who were the main custodians of patient monitoring. Thus, in agreement with existing literature, the feasibility study identified the need for EWS implementation, underscoring the requirement for contextualization, local validation and impact assessment before full-scale adoption.

In the second phase of the project, we developed – for the first time, to the best of our knowledge – a diagnostic prediction model for severe maternal outcome (SMO: maternal death or near miss) among the general obstetric population in a low-resource setting, based on recommended methodology, using local data from these settings. The model had excellent screening characteristics for SMO, and maintained good discriminatory power across all our internal validation data sets (area under ROC curves consistently above 90%). This model was used to develop a simple score-based EWS chart that consisted of seven clinical parameters (respiratory rate, temperature, systolic blood pressure, pulse rate, consciousness level, urine output and delivery mode for post-partum patients) that are easy to

measure with readily available patient monitoring tools. This is new evidence generated through this research, and it helps to clearly show how the EWS model generated from secondary records of obstetric admissions to Nigerian tertiary hospitals can provide an invaluable context-specific triaging tool for obstetric morbidity and mortality in low- and middle-income countries such as Nigeria.

Following implementation of the designed EWS in the last phase of the PhD project, there was a significant improvement in the frequency of monitoring and recording of vital signs (temperature, pulse, respiratory rate and blood pressure) in the intervention, but not in any of the control healthcare facilities. Although there was a significant reduction in the caesarean birth rate (from 39.9% to 31.5%), it was difficult to attribute this to EWS implementation given that other quality improvement programmes (EmOC training: assisted vaginal delivery, caesarean section and perioperative care) took place concurrently with the EWS implementation in the intervention hospital. Also, we could not attribute this to reduction in unnecessary CS as individual-level analysis of indications for CS was not conducted due to resource constraints. This is potentially a suitable research question to be explored in future research studies.

Although, opinion of clinical staff regarding EWS was positive, this did not translate into good usage rate of the chart among nurses and midwives. Challenges included feeling that the training provided was inadequate, stressing the need for training and retraining given that nurses and interns keep rotating in and out of the maternity units. Additionally, in agreement with the existing literature, shortages of trained staff and insufficient patient monitoring equipment and medical consumables were major challenges to effective patient monitoring in all our study sites.

Findings from this research showed that the obstetric EWS can improve the quality of patient care through better monitoring frequency and medical review based on abnormally high EWS scores. The EWS developed could be used to evaluate quality of patient care through assessing whether trigger events result in clinical action (doctor's review), and assessing timeliness of clinical action/medical intervention. Surveillance of patients who trigger action could allow for further evaluation and

discussion of quality of care, for example at maternal morbidity and mortality meetings. Obstetric EWS could also provide an invaluable tool for clinical audits and maternal death reviews.

Finally, the implementation phase was not without challenges. But overall, with staff education on usefulness of EWS, modifications to suit the setting, coupled with continuous training and retraining, it is feasible to implement obstetric EWS as a potentially acceptable patient monitoring tool to cope with the unique demands faced by obstetric practice in low-resource tertiary healthcare settings.

7.8. Unique contributions

The unique contributions of this PhD research to the body of knowledge on maternal monitoring are itemized below:

- This research provided an up-to-date synthesis of evidence on effectiveness of obstetric EWS as screening tools for morbidity and mortality (predictive accuracy) and in improving clinical outcomes in obstetric populations through a systematic review of literature (Umar, A., et al*.,* 2019). The review also provided evidence on the feasibility of implementing obstetric EWS in low-resource settings (Umar, A., et al*.,* 2019). This was the first published systematic review to report predictive accuracy of obstetric EWS for morbidity, and their effectiveness in improving clinical outcomes.
- To the best of our knowledge, this research reports for the first time an internally validated statistically developed diagnostic predictive model for obstetric morbidity and mortality among all women admitted to obstetric wards in a low-resource setting. This was developed using standardized model development methodology, and reported based on the TRIPOD statement (Collins et al., 2015a).
- This research demonstrated that the designed obstetric EWS was acceptable to healthcare workers and had the potential to improve the quality of patient care through improved monitoring frequency of vital signs and timely clinical review.
- This is the first report on implementation of obstetric EWS in any Nigerian tertiary hospital.

7.9. Recommendations

The preliminary findings of this study were used to advocate the introduction of an obstetric EWS in the maternity units of the University of Ilorin Teaching Hospital (the phase 3 intervention hospital). The local co-PI facilitated presentation of these findings (the feasibility, systematic review and phase 2 analysis) at the hospital's grand round in November 2018, which led to management approval of full-scale implementation of the coloured version of the EWS chart after the pilot study.

Overall, targeted key recommendations arising from this PhD research are as follows:

7.9.1. Policy and practice

- In implementing EWS at the facility level, consideration needs to be given to contextual challenges. Efforts should be made to address potential bottlenecks to effective implementation from the outset. These should include, but not be limited to, addressing human resources for health shortages, ensuring sufficient patient monitoring equipment and ensuring all maternity staff receive adequate training on EWS use.
- Hospital managements should modify staff deployment/rotation practices. Specifically, management should ensure mandatory induction and training of newly deployed staff into the maternity units that includes training on use of the EWS.
- As a long-term recommendation, training curricula for nursing, midwifery and possibly medical education should be revised to include the use of EWS for maternal monitoring. In this way, EWS would be seen as part of routine medical care and a quality improvement measure, not as profit-making research as perceived by some participants in phase 3 of this project (by comparing EWS implementation to incentives given during drug and pain studies by pharmaceutical companies). Additionally, this would provide a lasting solution to challenges constituted by staff rotation within clinical specialities.
- This thesis has established a strong evidence base supporting the usefulness of EWS in obstetric practice. Moving forward, the ideal design for large-scale implementation should be a stepped-wedge design.

7.9.2. Research

- Lack of standardization of the defining criteria for obstetric outcomes is a major challenge in most research studies on obstetric EWS, as reported in our systematic review (Umar, A., et al*.,* 2019). For instance, maternal morbidity was defined based on the CDC criteria in the study by Shields and colleagues (2016), while other studies (Austin et al., 2014; Singh S et al., 2016b; Singh S et al, 2012) defined morbidity based on consensus among authors. We therefore identified a need to standardize outcomes in EWS effectiveness studies for clinical and research purposes. We made efforts to address this in our phase 2 analysis by using a standardized definition for maternal near miss (Say et al*.,* 2009).
- Most of the published EWS studies were observational studies. Few were before–after studies, and so far only one of the published studies that assessed the effectiveness of EWS in improving clinical outcomes had death as a primary outcome (Aminu Umar et al*.,* 2019). Although this thesis reported no reduction in maternal deaths following EWS implementation, our intervention arm was a single facility with only 18 maternal deaths over the seven-month period of the research. More robust studies, preferably multicentre randomized controlled (or stepped-wedge) trials with large sample sizes, are required to evaluate the effectiveness of obstetric EWS in reducing maternal death.
- One limitation of the implementation and evaluation phase of this project was that it did not allow us to determine how often an EWS might have led to either delayed escalation due to low scores or unnecessary escalation due to high scores. This could be explored in future research.

Reflection

Reflecting on this PhD research and my positionality as a clinician, aspiring researcher and PhD candidate, I would first say that the whole process was indeed very challenging, yet a great and potentially rewarding learning experience. If I am to choose my PhD research topic over again, I definitely would have chosen the same! A lot went well as planned, a number of challenges were encountered and if I am to do it over again, I would have done few things differently.

Starting from the systematic review, the included studies have answered my research questions satisfactorily. My choice of methodology was great, although I would have collapsed similar outcome measures (morbidity and ICU admission, vital signs monitoring and pre-operative stabilization) to reduce heterogeneity and do a meta-analysis of studies on effectiveness of EWS on outcome.

The main approach I would not have done in the review was excluding studies of qualitative design. While this has significantly eased my analysis and reporting of the synthesised evidence, I do understand the potential drawback of missing evidence on contextual factors that could affect implementation of EWS. An ethnographic study I excluded from the review assessed value of a modified obstetric early warning system in managing maternal complications in the peripartum period (Mackintosh et al, 2012). Findings from this study suggests that, while the MEOWS has value in structuring the surveillance of hospitalised women with an established risk of morbidity, the complexities of managing risk and safety within the maternity pathway, the associated opportunity costs of MEOWS and variation in implementation currently call into question its role for routine use. These findings could checkmate the overly positive reports on the usefulness of EWS by the quantitative studies included in the review. It can also illuminate on the contextual challenges relating to low uptake of EWS encountered in the third phase of this PhD.

Going forward, the feasibility study was a multi-method designed study that involved observation, key informant interviews, focus group discussion and review of records. Although my observation was supposed to be non-participant as a researcher, an incident happened while I was observing midwives perform their

patient monitoring activities in one of the three feasibility site which I would like to reflect on here. A patient presented with antepartum haemorrhage secondary to placental abruption with live baby. The doctor on call was busy attending to other emergencies. Although my aim was to observe as unobtrusively as possible, I felt my intervention was direly needed, so did not hesitate to offer a helping hand to save her life, for two reasons; first, I am a medical doctor licenced by the Nigerian Medical and Dental Council (MDCN), and by the revised physician's oath (68th WMA Chicago USA, Oct 2017), I have pledged to maintain the utmost respect for human life, placing the health and wellbeing of patients as my first priority in all situations. Being that the feasibility study is going to be performed in Nigerian hospitals where I am licensed to practice, refusing to offer help under such situations is akin to breech of the Hippocratic oath.

Secondly, according to the ethical principles and guidelines for the protection of human subjects of research (Belmont report, 1979), the principles of beneficence and non-maleficence must be strictly adhered to in all research studies involving human subject. Both principles emphasized on maximizing benefit to participants and minimizing harm. Although the imminent catastrophe that might have resulted in that scenario (maternal and possibly newborn mortality) are not direct consequences of the research, I felt, refusing to offer help breeches both ethical principles. Thus, I spoke to the consultant on call on the phone who consented for me to intervene to save life. If I am faced with a similar scenario in the future, I would still do the same.

In terms of the design and validation of obstetric EWS for use in low resource settings (phase 2), most of this research phase went as planned. If the funding for this PhD were more generous, I would have made this phase a more robust case-control study by collecting controls from across all 42 Nigerian tertiary hospitals that partook in the near-miss study. This would address the limitation of over optimistic performance of the model from higher cases to controls ratio. I also would have matched cases and controls at individual level for both common demographic (such as age, socioeconomic status, place of residence and distance

to health facility) and obstetric characteristics (such as gravidity and parity) to adjust potential confounding factors.

Reflecting on the implementation and evaluation phase of this project, I would say this was the most challenging phase of the PhD research. In terms of time, energy and resource commitment, this phase was the most overwhelming of the three phases. We had strong support from the hospital authority, who made it a decree to use EWS by dispatching circulars to all obstetric wards (emergency, antenatal, postnatal medical, postnatal surgical and gynaecology wards) directing ward heads to adopt the EWS chart in place of routine vital signs charts for all obstetric inpatients. The implementation was also made to be primarily driven by the local implementation team. Sadly, however, the usage rate was not quite encouraging. Although this was blamed on a number of challenges during the qualitative activities, there could be more underlying contextual factors that could have contributed to the low uptake which might have been possibly missed. Understanding of usefulness of EWS might still be sub-optimal despite the training provided as reported by the feasibility study.

Having mentioned the above however, being a major change to what has been the organizational norm in terms of patient monitoring, the explanation to our findings of low EWS uptake may not be farfetched. Whilst many organisations appreciate the need for change, as many as 70% of the change programmes have been shown to not achieve their intended outcomes (Balogun and Hope Hailey, 2004). Fundamental to the success of organisational change, such as the intervention in this research, is the acceptance of the change by employees (the nurses and midwives). Within this context, the work of Kubler-Ross (1973), who argued that all humans go through 5 stages of 'grief' (denial, anger, bargaining, depression and acceptance) when faced with a loss or change, has been seen as relevant and has been applied to the management of organisational change (Bernard M et al 2010).

Wiggins (2009) uses the Kubler-Ross model to help guide communication and support during the period of change, which she suggests should be tailored to the stage of change that the employees have reached (Bernard M et al 2010). Of relevance to this research going forward is the need, as she suggests, for the nurses

and midwives to be given information to tackle their denial. Within the context of this research, this information could be the established usefulness of obstetric EWS as screening tools for morbidity, and their effectiveness in improving health outcomes as demonstrated by our published systematic review (Aminu Umar et al, 2019). Once the information has sunk in and they experience anger, bargaining and depression, they require various kinds of support. Once employees have begun accepting the situation they need a vision to put their commitment into (Bernard M et al 2010). Going forward, it would be important to ensure employees have successfully transitioned through denial to acceptance before full implementation.

One of the other influential perspectives within what are known as 'planned approaches' to change, that could be employed perhaps in the feature EWS implementation, is that of Lewin who argued that change involves a three stage process: firstly, unfreezing current behaviour; secondly, moving to the new behaviour; and, finally, refreezing the new behaviour (Todnem R, et al 2005). The three-step model was adopted for many years as the dominant framework for understanding the process of organisational change (Todnem, 2005; Fernandez & Rainey, 2006). To put in context, we presented the findings of our feasibility study and the systematic review during the grand round meeting of the obstetric department pre-implementation in the intervention hospital as an evidence base to unfreeze current practice of patient monitoring. We trained staff on the use of EWS and provided a mechanism to support and supervise implementation of the new behaviour (EWS implementation in this case). As part of the plans going forward, we intend to publish and disseminate our findings to the intervention hospital to enhance refreezing this new behaviour. Future EWS implementation should however improve upon these to be more organised and systematic with specific steps to unfreeze current monitoring practices, move to the EWS, then refreeze this new practice of patient monitoring (Todnem R, et al 2005).

Finally, reflecting on positionality of the research team, especially in the last Ph.D phase, the nature of qualitative research sets the researcher as the data collection instrument (Hooks, 1990). The researcher's beliefs, political stance, cultural background and professional inclination have been demonstrated to be important

variables that may affect the research process (Bourke B, 2014). Being doctors, professional barrier can potentially limit the ability of the research team to conveniently position themselves within the context of a major category of the researched (nurses and midwives in this case). Hence, I acknowledge that this might have influenced the way I accounted for the experiences, of these research subjects, about the implementation ad their challenges of using obstetric EWS.

Moreover, I noted a significant inconsistency between the observed EWS usage rate and reported staff experience, as was previously reported for partograph in similar setting in Nigeria (Opiah et al, 2012). Some of the responses we got sounded rather normative. Reflecting on these responses, despite attempt to be non-judgemental and reassure participants on this, I reckon the professional barrier between the interviewers (doctors) and the interviewees/FGD participants (nurses and midwives) could have contributed to this. As such, If I am to do this over, I would have nurse research assistants to convene at least the FGD sessions. Getting more nurses and midwives to derive such implementation has been found to be effective in other settings (Yazdizadeh et al, 2011; Teate A et al, 2013).

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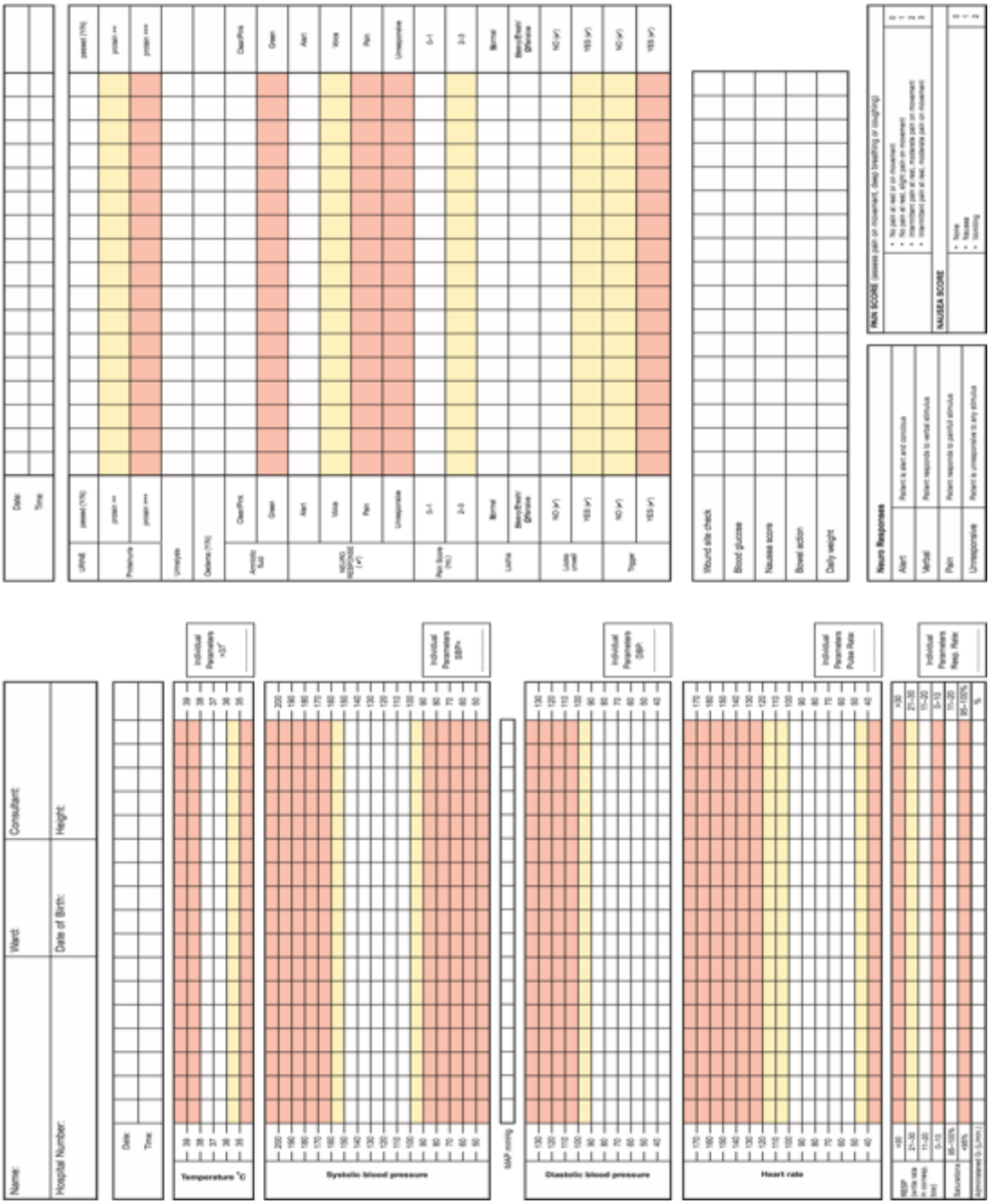
Annexes

Chapter 1 Annexes

Annex 1A: CEMACH MEOWS



Appendix 1B: Summary of role of the candidate

Study phase	Activity	Responsibility	Additional input
Background/Formative phase	Conceptualization	**Aminu Umar,** Charles Ameh	Matthews Mathai and Helen Allot
	Preliminary review of literature	**Aminu Umar,** Charles Ameh	Matthews Mathai and Helen Allot
	Concept note preparation	**Aminu Umar**	Charles Ameh, Matthews Mathai
	Observation at Liverpool Women's Hospital (One week)	**Aminu Umar**	Facilitated by Helen Allot, Charles Ameh and Saladin Sawan
	Presentation and feedback from CMNH Academic team	**Aminu Umar**	CMNH academic team especially Hellen Allot, Alexander Manu, Helen Nabwera, Mamuda Aminu and Florence Mgawadere
Systematic review	Conceptualisation of the review	**Aminu Umar,** Charles Ameh, Matthews Mathai	Francis Muriithi, Mamuda Aminu
	Designing the protocol	**Aminu Umar**	Charles Ameh, Matthews Mathai
	Registration with PROSPERO	**Aminu Umar**	Francis Muriithi, Mamuda Aminu
	Conduct of the review	**Aminu Umar,** Francis Muriithi	Charles Ameh, Matthews Mathai, Mamuda Aminu
	Presentation at academic team	**Aminu Umar,** Charles Ameh	CMNH Academic team members
	Producing first manuscript draft	**Aminu Umar**	
	Review and input to early drafts	Charles Ameh, **Aminu Umar**, Francis Muriithi, Matthews Mathai	
	Co-ordination of drafts and finalisation of paper	Charles Ameh, **Aminu Umar**	Matthews Mathai
	Submission of final draft, reviews of correction till manuscript acceptance	Charles Ameh, **Aminu Umar**	Matthews Mathai

	Chapter write up and review	**Aminu Umar**	Charles Ameh, Matthews Mathai
Phase one *Feasibility study*	Designing the study	**Aminu Umar,** Charles Ameh, Matthews Mathai	Alexander Manu, Helen Nabwera, Helen Allot, Helen Smith
	Producing study protocol and data collection tools	**Aminu Umar,** Charles Ameh, Matthews Mathai	Helen Allot, Alexander Manu, Helen Nabwera, Mamuda Aminu
	Ethics application at LSTM and In-country	**Aminu Umar,** Charles Ameh	Mamuda Aminu, Abimbola Olaniran, Adura Banke-Thomas, Idris Liman (NHA Abuja), U. S Bawa (ABUTH Zaria), Hajara Ismail (specialist hospital Bauchi)
	Data collection	**Aminu Umar**	Research assistants: Naima Mohammed and Halidu Mohamed (NHA), Naima Mohammed and Tanimu Halilu (ABUTH Zaria), Naima Mohammed and Buhari Tafida (specialist hospital Bauchi)
	Data management and analysis	**Aminu Umar**	Charles Ameh, Matthews Mathai, Thidar Pyone, Alex Manu, Sarah White
	Presentation at academic team	**Aminu Umar,** Charles Ameh	CMNH Academic team members
	Chapter write up and review	**Aminu Umar**	Charles Ameh, Matthews Mathai
	Producing first manuscript draft	**Aminu Umar**	
	Review and input to early draft	Charles Ameh, **Aminu Umar**, Matthews Mathai	
	Co-ordination of drafts and finalisation of paper	Charles Ameh, **Aminu Umar**	Matthews Mathai

	Submission of final draft, reviews of correction till manuscript acceptance	**Aminu Umar**	Charles Ameh, Matthews Mathai
Phase 2 *Design and internal validation of EWS model and score-based chart*	Conceptualisation of phase	**Aminu Umar**	Charles Ameh, Matthews Mathai, Alexander Manu
	Protocol and ethics clearance	**Aminu Umar**	Charles Ameh, Matthews Mathai, Olufemi Taiwo Oladapo (WHO), Idris Liman (NHA Abuja), US Bawa (ABUTH Zaria), Calvin Chama (ATBUTH Bauchi)
	Securing maternal death and Near-miss case data set	**Aminu Umar,** Charles Ameh, Matthews Mathai	Olufemi Taiwo Oladapo (WHO Geneva) and Nigeria Maternal near-miss surveillance network
	Control data collection	**Aminu Umar**	Research assistants: Naima Mohammed, and Halidu Mohamed (NHA), Naima Mohammed and Tanimu Halilu (ABUTH Zaria), Naima Mohammed and Buhari Tafida (ATBUTH Bauchi)
	Data management and analysis	**Aminu Umar,** Alexander Manu	Charles Ameh, Matthews Mathai, Sarah White
	Conversion of EWS Model to a score based monitoring chart	**Aminu Umar,** Charles Ameh, Matthews Mathai	Helen Allot, Hannah McCauley, Florence Mgawadere, Terry Kana, Fiona Dickinson
	Presentation and input from academic team	**Aminu Umar**	CMNH Academic team members
	Producing first manuscript draft	**Aminu Umar**	
	Review and input to early drafts	**Aminu Umar**, Alexander Manu, Charles Ameh, Matthews Mathai	

	Co-ordination of drafts and finalisation of paper	Charles Ameh, **Aminu Umar**	Alexander Manu, Matthews Mathai
	Submission of final draft, reviews of correction till manuscript acceptance	Charles Ameh, **Aminu Umar**	Alexander Manu, Matthews Mathai
	Chapter write up and review	**Aminu Umar**	Charles Ameh, Matthews Mathai
Phase 3 *Implementation and external validation*	Conceptualisation of phase	**Aminu Umar**	Charles Ameh, Matthews Mathai, Alexander Manu
	Baseline data for sample size estimate	Charles Ameh, **Aminu Umar**	Hauwa Mohammed (LSTM Nigeria), Munirdeen Ijaiya and Sabi Ibrahim (UITH Ilorin)
	Finalising study protocol	**Aminu Umar,** Charles Ameh, Matthews Mathai	Alexander Manu, Sarah White, Munir-deen Ijaiya
	Ethics application LSTM and In-country	**Aminu Umar**	Munirdeen Ijaiya (UITH, Ilorin), Idris Liman (NHA Abuja) and Calvin Chama (ATBUTH Bauchi)
	CEmOC training including demonstration of MEOWS in UITH Kwara	CMNH Emergency Obstetric Care team	**Aminu Umar,** Hauwa Mohammed, Munirdeen Ijaiya, UK volunteers (obstetricians and anaesthesiologists)
	Implementation of EWS in UITH Kwara	**Aminu Umar**	Munirdeen Ijaiya, Balogun A. O (Head obstetrics and gynaecology UITH Kwara), Sabi Ibrahim, Sadiya Gwadabe
	Surveillance and quality audit	**Aminu Umar**	Munirdeen Ijaiya, Sabi Ibrahim, Sadiya Gwadabe
	Data collection (baseline and post implementation)	**Aminu Umar**	Research assistants: Naima Mohammed and Halidu Mohamed (NHA), Naima Mohammed and Buhari Tafida (ATBUTH

		Bauchi), Naima Mohammed, Sabi Ibrahim and Sadiya Gwadabe (UITH Kwara)
Data management and analysis	**Aminu Umar**	Charles Ameh, Matthews Mathai, Alexander Manu
Producing first manuscript drafts (protocol and external validation papers)	**Aminu Umar**	
Review and input to early drafts	Charles Ameh, **Aminu Umar**, Matthews Mathai	
Co-ordination of drafts and finalisation of papers	**Aminu Umar**	Alexander Manu, Charles Ameh, Matthews Mathai, Munirdeen Ijaiya, Sabi Ibrahim, Idris Liman and Calvin Chama
Submission of final draft, reviews of correction till manuscript acceptance	**Aminu Umar**	Alexander Manu, Charles Ameh, Matthews Mathai
Chapter write up and review	**Aminu Umar**	Charles Ameh, Matthews Mathai

Annex 1C: Characteristics of research team

Name	Background	Position/Role	Qualifications	Research experience
Dr Aminu Umar	Clinician/research	Ph.D Candidate	MBBS, MPH	Managed PhD project
Dr Charles Ameh	Obstetrician/research	Lead supervisor	MBBS, MPH, DRH, PH.D	Research in LMICs
Prof M Mathai	Obstetrician/research	Co-supervisor	MBBS, MD, PH.D	Research in LMICs
Prof C. Chama	Obstetrician	Co-PI ATBUTH	Professor of Obstetrics	Clinical research
Prof M Ijaiya	Obstetrician	Co-PI UITH	Professor of Obstetrics	Clinical research
Dr I Liman	Obstetrician	Co-PI NHA	Consultant Obstetrician	Clinical research
Dr Sabi Ibrahim	Trainee Doctor	Member LIT	Senior registrar	Limited
Dr S Gwadabe	Trainee Doctor	Member LIT	Registrar	Masters project
Tanimu Mohammed	Clerical staff	Research assistant	Non-medical	Data analyst in ABUTH
Sadiya Yusuf	CNO	Member LIT	RNRM	Limited
Buhari Abdullahi	Physiotherapist	Research assistant	MSc Physiotherapy	Masters project
Naima Mohammed	Medical student	Research assistant	Medical student	Limited
Halidu Mohammed	Record staff	Research assistant	Medical record	Data analyst in NHA

PI: Principal investigator CNO: Chief Nursing Officer LIT: Local Implementation Team RNRM: Regitered Nurse Midwife

Chapter 2 Annexes

Annex 2A (Published systematic review protocol):

Aminu Umar, Francis Muriithi, **Charles Ameh and Matthews Mathai, Systematic review of literature on early warning systems for use in Obstetric population: review protocol,**

PROSPERO 2017(link is external).

Annex 2B: Spreadsheet for systematic review studies selection

Attached MS excel spreadsheet

Appendix 2C: QUADAS-2 assessed quality of individual studies

Study	RISK OF BIAS				CONCERN ABOUT APPLICABILITY		
	Patient selection	Index test	Reference standard	Participants flow	Patient selection	Index test	Reference standard
Singh S et al, 2012	L	L	H	L	L	L	L
Carle C et al, 2013	L	L	L	U	L	L	U
Singh A et al, 2016	L	L	H	L	L	L	U
Hedriana HL et al, 2016	U	L	U	L	L	L	H
Ryan HM et al, 2017	L	L	H	L	L	L	L
Paternino-Caicedo et al, 2017	U	L	L	L	L	L	L
Edwards ES et al, 2007	U	L	L	H	L	L	L
Lappen RJ et al, 2010	U	U	L	H	L	H	U
Von-Dadelszen P et al, 2011	L	L	U	L	L	H	U
Payne BA et al, 2014	L	L	U	L	L	H	U
Nathan HL et al, 2017	L	U	H	L	L	U	H
Austin DM et al, 2013	H	L	U	L	L	U	U
Maguire PJ et al, Karen AP 2015	L	L	U	U	L	L	U
Maguire PJ, Amy C.O et al, 2015	L	L	U	H	L	L	U

Shields E L et al 2016	L	L	U	H	L	L	L
Sheikh S et al, 2017	L	H	U	L	L	H	U
Merriel A et al, 2017	U	L	U	L	L	L	U

Chapter 3 Annexes

Annex 3A: Full LSTM ethics approval for phase one (feasibility study)

Mr Aminu Umar
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool
L3 5QA

LSTM
LIVERPOOL SCHOOL OF TROPICAL MEDICINE
Pembroke Place,
Liverpool, L3 5QA, UK
Tel: +44(0)151 705 3100
Fax: +44(0)151 705 3370
www.lstmed.ac.uk

Monday, 20 November 2017

Dear Mr Umar,

Research Protocol (17-047) Early warning system to improve maternal health in Nigeria; design, validation and evaluation of modified obstetric early warning chart for use in resource limited settings

Thank you for your correspondence of 17 November 2017 providing the necessary in-country approvals for this project. I can confirm that the protocol now has formal ethical approval from the LSTM Research Ethics Committee.

The approval is for a fixed period of three years and will therefore expire on 19 November 2020. The Committee may suspend or withdraw ethical approval at any time if appropriate.

Approval is conditional upon:

- Continued adherence to all in-country ethical requirements.
- Notification of all amendments to the protocol for approval before implementation.
- Notification of when the project actually starts.
- Provision of an annual update to the Committee.
  Failure to do so could result in suspension of the study without further notice.
- Reporting of new information relevant to patient safety to the Committee
- Provision of Data Monitoring Committee reports (if applicable) to the Committee

Failure to comply with these requirements is a breach of the LSTM Research Code of Conduct and will result in withdrawal of approval and may lead to disciplinary action. The Committee would also like to receive copies of the final report once the study is completed. Please quote your Ethics Reference number with all correspondence.

Yours sincerely

Dr Angela Obasi
Chair
LSTM Research Ethics Committee

Annex 3B: Full LSTM ethics approval for Phase 3

Dr Aminu Aliyu Umar
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool
L3 5QA

LSTM
LIVERPOOL SCHOOL OF TROPICAL MEDICINE
Pembroke Place,
Liverpool, L3 5QA, UK
Tel: +44(0)151 705 3100
Fax: +44(0)151 705 3370
www.lstmed.ac.uk

Wednesday, 21 November 2018

Dear Dr Umar,

Research Protocol (18-074) Implementation and evaluation of obstetric early warning chart in a low resource tertiary healthcare setting

Thank you for your letter of 19 November 2018 providing the necessary in-country approvals for this project. I can confirm that the protocol now has formal ethical approval from the LSTM Research Ethics Committee.

The approval is for a fixed period of three years and will therefore expire on 20 November 2021. The Committee may suspend or withdraw ethical approval at any time if appropriate.

Approval is conditional upon:

- Continued adherence to all in-country ethical requirements.
- Notification of all amendments to the protocol for approval before implementation.
- Notification of when the project actually starts.
- Provision of an annual update to the Committee.
  Failure to do so could result in suspension of the study without further notice.
- Reporting of new information relevant to patient safety to the Committee
- Provision of Data Monitoring Committee reports (if applicable) to the Committee

Failure to comply with these requirements is a breach of the LSTM Research Code of Conduct and will result in withdrawal of approval and may lead to disciplinary action. The Committee would also like to receive copies of the final report once the study is completed. Please quote your Ethics Reference number with all correspondence.

Yours sincerely

Dr Angela Obasi
Chair
LSTM Research Ethics Committee

Annex 3C1: In country approval for feasibility study ABUTH Zaria

DEPARTMENT OF OBSTETRICS & GYNECOLOGY
AHMADU BELLO UNIVERSITY TEACHING HOSPITAL
ZARIA-NIGERIA

Chief Medical Director: **PROF. LAWAL KHALID,** MBBS, FWCS, FWACS, FRCS(ED), mni
Chairman, Medical Advisory Committee: **PROF. ADAMU AHMED,** MBBS (ABU), BI, FWACS, FICS, FACS
Ag. Director of Administration: **MRS. M. BEZUM,** BA Pub. Admin., MPA (ABU, Zaria)
Head of Department: **DR. U.S. BAWA,** MBBS (UNIMAID), FWACS

Telephone: Zaria 069-332271-5
Fax: Zaria 069-332688
E-mail: abuth@anpa.net.ng
Postal Address:
Department of Obstetrics & Gynaecology
A.B.U. Teaching Hospital,
P.M.B. 1026, Zaria-Nigeria.

25[th] September, 2017.

Centre for Maternal & Newborn Health,
Department of International Public Health,
Liverpool School of Tropical Medicine,
United Kingdom.

To Whom it May Concern

Dear Sir/Madam,

Approval for Dr. Aminu Aliyu Umar

I write to convey the approval of the Obstetrics and Gynaecology Department, Ahmadu Bello University Teaching Hospital Zaria for Dr. Aminu Aliyu Umar to conduct a feasibility study in our unit.

While thanking you for selecting our facility for the study, please accept my best regards.

Yours faithfully,

Dr. U.S. Bawa,
Head of Obstetrics & Gynaecology.

Annex 3C2: In country approval for feasibility study NHA Abuja

obgyn_nationalhospital@yahoogroups.com

National Hospital Abuja
Department of Obstetrics & Gynaecology

23rd August, 2017

The Centre for Maternal & Newborn Health,
Department of International Public Health,
Liverpool School of Tropical Medicine,
United Kingdom.

TO WHOM IT MAY CONCERN

Dear Sir/Madam,

RE- Dr. AMINU ALIYU UMAR (STUDENT NUMBER 202259932)

I write to convey the approval of the Obstetrics and Gynaecology Department, National Hospital, Abuja for the above named PhD student to conduct a one week feasibility study in our department.

We thank you for selecting our hospital for this study.

Yours faithfully,

Dr. F.Z. Mairami
HOD Obstetrics & Gynaecology

Plot 132, Central District (Phase II), P.M.B 425, Garki - Abuja, Nigeria
Telephone: +234-9-2342686, 2341224, 2341382, 6712524, Fax: 234-9-2342632

Annex 3C3: In country approval for feasibility study Bauchi

SECRET

BAUCHI STATE SPECIALIST HOSPITAL BOARD

P.M.B. 005,
Specialist Hospital, Bauchi,
☎:077-542897

Our Ref: SHB/ADM/41/V.I

Your Ref: _____

Date: 8th September, 2017

Dr. Charles A. Ameh
Centre for Maternal and Newborn Health,
Department of International Public Health,
Liverpool School of Tropical Medicine,
United Kingdom

Dear Sir,

APPROVAL FOR DR. AMINU ALIYU UMAR,
STUDENT NUMBER 20/259932

I write to convey the approval of the management of Specialist Hospital, Bauchi for Dr. Aminu Aliyu Umar to conduct a feasility study within one week in our Hospital.

We thank you for selecting our Hospital for the study.

Yours faithfully,

DR. HABIBA ISMAIL IBRAHIM
CMAC

Annex 3D1: In country approval for phase 3 UITH

UNIVERSITY OF ILORIN TEACHING HOSPITAL

Chairman:
OLOROGUN O'TEGA EMERHOR (ODN)

Chief Medical Director:
PROF. A. D. YUSSUF
MBBS, FCMPsych, Cert. HP & Mgt, MCH, FILA, FAZA

Ag Chairman Medical Advisory Committee:
DR (MRS) A. O. SAKA
MBBS, FCMPaed, MPH, Cert. HP & Cert NMS

Director of Administration:
MR. D. S. ODAIBO
B. A. (Hons) MLR, MNIM, MCIA

Old Jebba Road, Oke-Ose,
P.M.B. 1459, Ilorin,
Kwara State, Nigeria.

E-mails:
- unithilorin1980@yahoo.com
- info@uith.org

Telephone:
- 08055763942

UITH ERC Protocol Number: ERC PIN/2018/09/0696
UITH ERC Approval Number: ERC PAN/2018/11/1843

Our Ref: UITH/CAT/189/19^A/967 **Date:** 06/11/2018

IMPLEMENTATION AND EVALUATION OF OBSTETRIC EARLY WARNING CHART IN A LOW RESOURCE TERTIARY HEALTHCASE SETTING

UITH Ethical Research Committee (ERC) assigned number: NHREC/02/05/2010
Name of Applicant/Principal Investigator: Dr. Aminu Aliyu Umar
Address of Applicant: Center for Maternal & Newborn Health, Liverpool School of Tropical Medicine
Date of receipt of application: 16/09/2018
Type of Review: Full Committee Review
Date of full Committee Decision on the Research: 26/09/2018
Date of full Committee approval: 06/11/2018

Notice of full Committee Approval

I am pleased to inform you that the research described in the submitted protocol, the consent forms and other participant information materials have been reviewed by the UITH Ethical Review Committee (ERC) and given full Committee approval.

This approval dates from 06/11/2018 to 05/11/2019. You are requested to inform the committee at the commencement of the research to enable it appoint its representative who will ensure compliance with the approved protocol. If there is delay in starting the research, please inform the ERC so that the dates of approval can be adjusted accordingly.
Note that no participant accrual or activity related to this research may be conducted outside these dates.

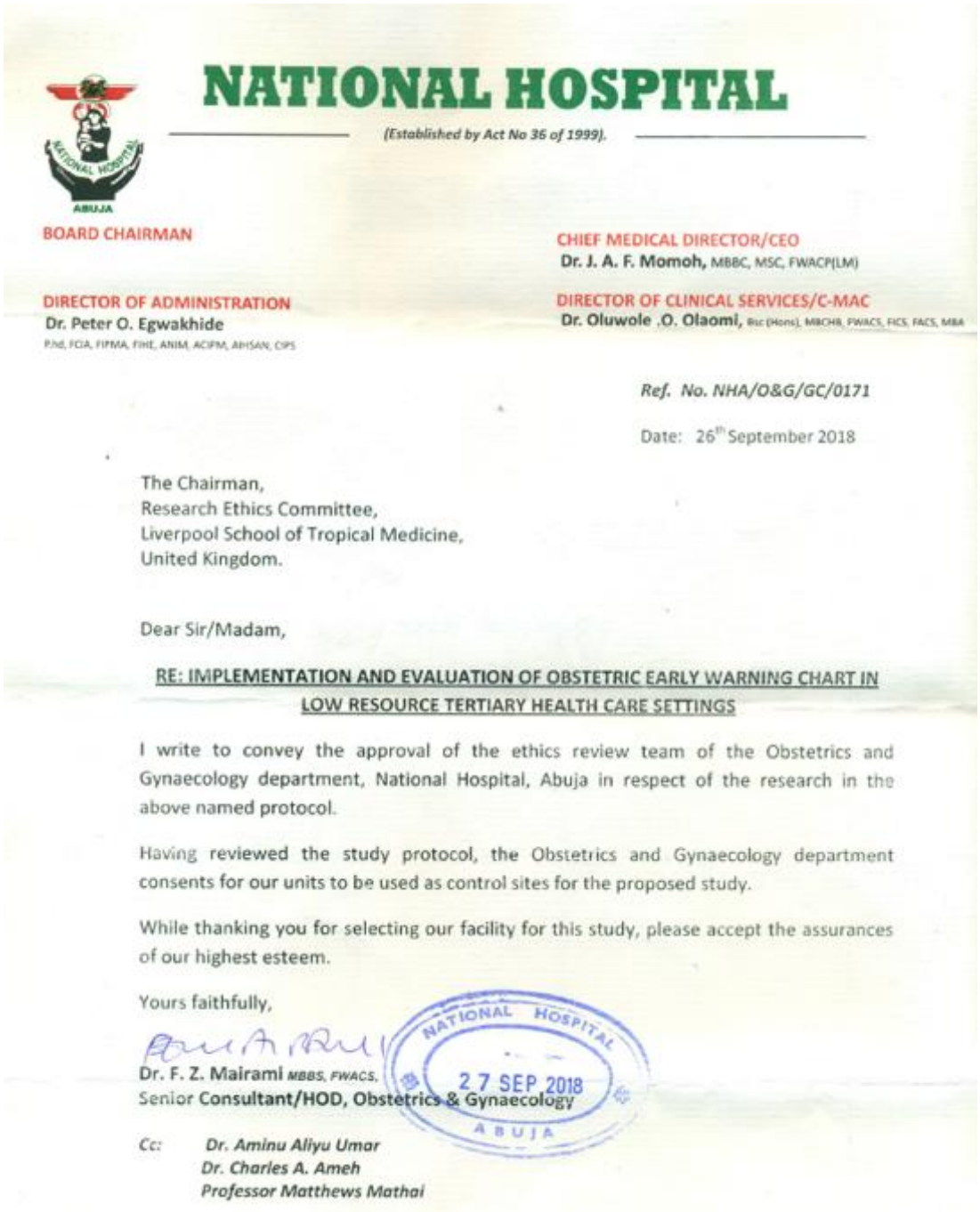
The UITH ERC requires you to comply with all the institutional guidelines and regulations and ensure that all adverse events are reported promptly to the ERC.
No changes are allowed in the research without prior approval by the ERC. Please note that the ERC reserves the right to conduct monitoring/oversight visit to your research site without prior notification.

Notwithstanding above, we will not be responsible for any misconduct on the part of the researcher in the course of carrying out the research.

Thank you

PROF. (MRS.) F.O. ADEPOJU MBBS,MSC,FMCOPH,FWASC,FICS,MNIM
Chairman, UITH Ethics Review Committee. (ERC)

Annex 3D2: In country approval for phase 3 Abuja



NATIONAL HOSPITAL

(Established by Act No 36 of 1999).

ABUJA

BOARD CHAIRMAN

CHIEF MEDICAL DIRECTOR/CEO
Dr. J. A. F. Momoh, MBBC, MSC, FWACP(LM)

DIRECTOR OF ADMINISTRATION
Dr. Peter O. Egwakhide
PhD, FCIA, FIPMA, FIHE, ANIM, ACIPM, AHSAN, CIPS

DIRECTOR OF CLINICAL SERVICES/C-MAC
Dr. Oluwole .O. Olaomi, Bsc (Hons), MBCHB, FWACS, FICS, FACS, MBA

Ref. No. NHA/O&G/GC/0171

Date: 26th September 2018

The Chairman,
Research Ethics Committee,
Liverpool School of Tropical Medicine,
United Kingdom.

Dear Sir/Madam,

RE: IMPLEMENTATION AND EVALUATION OF OBSTETRIC EARLY WARNING CHART IN LOW RESOURCE TERTIARY HEALTH CARE SETTINGS

I write to convey the approval of the ethics review team of the Obstetrics and Gynaecology department, National Hospital, Abuja in respect of the research in the above named protocol.

Having reviewed the study protocol, the Obstetrics and Gynaecology department consents for our units to be used as control sites for the proposed study.

While thanking you for selecting our facility for this study, please accept the assurances of our highest esteem.

Yours faithfully,

NATIONAL HOSPITAL 27 SEP 2018 ABUJA

Dr. F. Z. Mairami *MBBS, FWACS,*
Senior **Consultant/HOD, Obstetrics & Gynaecology**

Cc: Dr. Aminu Aliyu Umar
Dr. Charles A. Ameh
Professor Matthews Mathai

Annex 3D3: In country approval for phase 3 ATBUTH Bauchi

ABUBAKAR TAFAWA BALEWA UNIVERSITY TEACHING HOSPITAL, BAUCHI
Hospital Road Off Yandoka Street, P.M.B 0117, Bauchi
E-mail: mails4atbuthbauchi@gmail.com

Chairman, Governing Board
Zacch Adedeji, FCA

Chief Medical Director
Dr. Mohammed Alkali BM, BCH, FWACP
(Gastoenterologist)

Our Ref: ATBUTH/ADM/4 2/VOL.I

Date: 24th September 2018

Dr. Aminu Aliyu Umar

RE: IMPLEMENTATION AND EVALUATION OF OBSTETRIC EARLY WARNING CHART IN A LOW RESOURCE TERTIARY HEALTHCARE SETTING
ATBUTH (REC) Assigned Number – 0027/2018
Date of Approval: 24th September 2018
Address of Researcher: Center of Maternal and Newborn Health Liverpool School of tropical medicine Pembroke place, L35QA, Liverpool, United kingdom
Email: Charles.ameh@ismed.ac.uk
GSM: +44157053706

RE: *NOTICE OF FULL APPROVAL*

This is to inform you that the research in the submitted protocol, the consent forms and other vital documents have been reviewed and given full committee approval from 24th September 2018 to 24th September , 2019. If there is any delay in starting the research please inform REC so that the date can be adjusted accordingly. Note that participant accrual or activity related to this research should not be conducted outside these days.

All informed consent forms used in the study must be carrying the assigned REC number and the duration of REC approval of the study. The national code for Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations and with the tenants' of the code including ensuring that all adverse events are reported promptly to REC. No changes are permitted in the research without prior approval by REC except in circumstances outlined in the code. The REC reserves the right to conduct compliance visit to your research site without prior notice.

25/9/18

Prof. Calvin Chama
Chairman Research & Ethics ATBUTH, Bauchi

Ag. Chairman, Medical Advisory Committee

Director of Administration

Annex 3E: LSTM ethics Waiver Phase 2

Mr Aminu Aliyu Umar
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool
L3 5QA

LSTM
LIVERPOOL SCHOOL OF TROPICAL MEDICINE
Pembroke Place,
Liverpool, L3 5QA, UK
Tel: +44(0)151 705 3100
Fax: +44(0)151 705 3370
www.lstmed.ac.uk

Friday, 27 July 2018

Dear Mr Umar

Research Protocol (17-047) 'Early warning system to improve maternal health in Nigeria; design, validation and evaluation of modified obstetric early warning chart for use in resource limited settings'

Thank you for your correspondence of 20 July 2018 providing the LSTM Research Ethics Committee and LSTM Research Governance Manager with details of a request for a waiver/ ethical clearance in respect of the second phase with the above-named title. This second phase involves analysis of anonymised secondary data.

This request has now been reviewed, noted and accepted on the behalf of the Committee and the LSTM, as study Sponsor. Please continue to adhere to the conditions of approval and to update us of any further changes to the study that may arise.

Yours sincerely,

Dr Angela Obasi
Chair
LSTM Research Ethics Committee

Yours sincerely,

Mr Carl Henry
LSTM Research Governance Manager
LSTM Research Governance and Ethics Office

Chapter 4 Annexes

Annex 4A: Phase 1 survey data collection tool

Hospital Name: _____ Date: _____

Section 1: Hospital annual records (events in the previous year)

1. Number of deliveries: _____

Months		A16	S16	O16	N16	D16	J17	F17	M17	A17	M17	J17	J17
Total admissions													
Booked													
Un-booked													
Booked elsewhere													
Term	Live births												
	Stillbirths												
Preterm	>32weeks												
	<32weeks												
Abortion													

2. Types of deliveries:

Types of delivery	Months											
	A16	S16	O16	N16	D16	J17	F17	M17	A17	M17	J17	J17
Normal SVD												
Vaginal breech												
ELCS												
EMCS												
Instrumental vaginal												
Vacuum												
Forceps												
Destructive												
others												

3. Number of maternal deaths: _____

Months	A16	S16	O16	N16	D16	J17	F17	M17	A17	M17	J17	J17
Maternal deaths												
Near misses												

4. Obstetric complications:

Categories	A16	S16	O16	N16	D16	J17	F17	M17	A17	M17	J17	J17
Obstetric haemorrhage												
Placenta Praevia												
Placental abruption												
Ruptured uterus												
Unclassified haemorrhage												
Ectopic pregnancy												
Vasa previa												
Pregnancy related infections												
Chorioamnionitis												
Puerperal genital sepsis												
Hypertensive disorders												
PIH												
Pre-eclampsia												
Eclampsia												
Chronic hypertension												
Prolonged labour												
Obstructed labour												
Thromboembolism												
Episiotomy/Tear												
Other complications												

A16 to J17: is August 2016, to July 2017.

2. Staffing level:
   - Nurses _____
   - Midwives _____

Annex 4B: Participant Information Sheet: Observed staff

Early warning System to improve maternal health in Nigeria: *Design, validation and evaluation of modified obstetric early warning chart for use in resource limited settings*

INVITATION TO TAKE PART IN A RESEARCH STUDY

Good day Sir/Madam!

My name is Aminu Aliyu Umar, I am a first-year postgraduate research degree student at the Centre for Maternal and New-born Health, Liverpool School of Tropical Medicine, University of Liverpool. I am conducting this brief study as part of my PhD research entitled "*Early warning system to improve maternal health in Nigeria, design, validation and evaluation of modified obstetric early warning chart for use in resource limited settings'.* I hereby cordially invite you to take part in this study. However, it is important that you know why the research is being done, and what it entails before deciding to take part. Kindly take time to go through this document carefully, discuss it with family or friends if you wish, and you are free to decide whether to take part or not.

PURPOSE OF THE STUDY

The need for this study arose from the high prevalence of maternal deaths in the developing countries, and especially in Nigeria; out of the 303,000 maternal deaths that occurred around the world in 2015, approximately twenty percent were contributed by Nigeria alone. Many of these deaths have been attributed to delay in recognizing complications of pregnancy and childbirth.

A clinical tool (obstetric early warning chart) is capable of recognizing women who are likely to benefit from an earlier life-saving intervention. This tool has been in use in the hospitals and maternities in the United Kingdom and other developed countries for over a decade now. Use of this tool in monitoring sick pregnant and delivered women has been proven to reduce maternal deaths and number of women suffering irreversible complications related to pregnancy and childbirth significantly. Thus, the overall aim of my project is to introduce and evaluate the use of obstetric early warning system for maternal monitoring in Nigerian hospitals.

To look at feasibility and predict possible problems with implementation of obstetric early warning chart in Nigeria, it was deemed necessary to conduct an initial pilot feasibility study in selected hospitals; this stage is where the study is at the moment. In this phase, we intend to conduct an observation of maternal care/treatment monitoring practices, conduct key informant interviews targeting senior midwives/nurses and, conduct focus group discussions with midwives who perform

monitoring of pregnant or recently delivered women in maternity, obstetric wards/high dependency units.

What is an obstetric early warning system

These are systems designed, for use in all obstetric inpatients, to track maternal physiological parameters, and to aid early recognition and treatment of the acutely unwell parturient. They assign weighted values to a few parameters (often six vital signs in most of the charts), according to their degree of deviation from normal, and define a threshold beyond which mandatory actions must be taken to prevent irreversible complications or death.

What is required of you

I will be sitting to observe you offer care to patients. Basically, I will be looking out for vital signs monitoring and recordings, clinical examinations and records, and interactions between you and the medical doctors in the course of patient management, particularly with regards to calling for review of patients when necessary. I can assure you that I am not here to pass judgement on your practice or clinical skills, so I urge you to feel free and discharge your duties as usual. The information I collect will be analysed and used to enable us to develop early warning chart that can be used within the context of hospitals in Nigeria and other similar developing countries. If you agree to be observed, I will require you to sign a written consent form.

TERMINATION OF PARTICIPATION

Your participation is voluntary, and you may decide to stop being a part of the study at any time without explanation and without penalty.

CONFIDENTIALITY/ANONYMITY

Please note that the following measures are going to be taken to ensure absolute anonymity and confidentiality in the conduct of the study.

- The data collected do not contain any personal information about you.
- No one will be able to link the data collected to your identity and name.
- The data will be seen only by the researchers and will not be made available to anyone else.

FOR FURTHER INFORMATION ABOUT THIS RESEARCH STUDY

I will be glad to answer your questions about this study at any time. You may contact me at aminu.umar@lstmed.ac.uk or First floor, Centre for Maternal and Newborn

Health, Wolfson building, Liverpool School of Tropical Medicine, Pembroke place, L3 5QA, Liverpool.

Annex 4B: Participant Information Sheet: Observed patients

Early warning System to improve maternal health in Nigeria: *Design, validation and evaluation of modified obstetric early warning chart for use in resource limited settings*

INVITATION TO TAKE PART IN A RESEARCH STUDY

Good day Sir/Madam!

My name is Aminu Aliyu Umar, I am a first-year postgraduate research degree student at the Centre for Maternal and New-born Health, Liverpool School of Tropical Medicine, University of Liverpool. I am conducting this brief study as part of my PhD research entitled "*Early warning system to improve maternal health in Nigeria, design, validation and evaluation of modified obstetric early warning chart for use in resource limited settings'.* I hereby cordially invite you to take part in this study. However, it is important that you know why the research is being done, and what it entails before deciding to take part. Kindly take time to go through this document carefully, discuss it with family or friends if you wish, and you are free to decide whether to take part or not.

PURPOSE OF THE STUDY

The need for this study arose from the large number of women dying from complications of pregnancy and child birth in the developing countries, and especially in Nigeria; out of the 303,000 maternal deaths that occurred around the world in 2015, approximately twenty percent were contributed by Nigeria alone. Many of these deaths have been attributed to delay in recognizing complications of pregnancy and childbirth.

A clinical tool (obstetric early warning chart) is capable of recognizing women who are likely to benefit from an earlier life-saving intervention. This tool has been in use in the hospitals and maternities in the United Kingdom and other developed countries for over a decade now. Use of this tool in monitoring sick pregnant and recently delivered women has been proven to reduce maternal deaths and number of women suffering irreversible complications related to pregnancy and childbirth significantly. Thus, the overall aim of my project is to introduce and evaluate the use of obstetric early warning system for monitoring of sick pregnant and recently delivered women in Nigerian hospitals.

To look at feasibility and predict possible problems with implementation of obstetric early warning chart in Nigeria, it was deemed necessary to conduct an initial feasibility study in selected hospitals; this stage is where the study is now.

What is required of you

I will be sitting to observe the medical staff offering care to you as they discharge their responsibility. Basically, I will be looking out for vital signs monitoring and recordings, clinical examinations and records, and interactions between the midwives/nurses and the medical doctors in the course of patient management. This information will be analysed and used to enable us to develop early warning chart that can be used within the context of hospitals in Nigeria and other similar developing countries. If you agree to be observed, I will require you to sign a written consent form.

TERMINATION OF PARTICIPATION

Your participation is voluntary, and you may decide to stop being a part of the study at any time without explanation and without penalty. I can also assure you in all honesty that your decision on whether to agree to be observed will not affect the care you, or your sick child will receive in this facility.

CONFIDENTIALITY/ANONYMITY

Please note that the following measures are going to be taken to ensure absolute anonymity and confidentiality in the conduct of the study.

- The data collected do not contain any personal information about you.
- No one will be able to link the data collected to your identity and name.
- The data will be seen only by the researchers and will not be made available to anyone else.

FOR FURTHER INFORMATION ABOUT THIS RESEARCH STUDY

I will be glad to answer your questions about this study at any time. You may contact me at aminu.umar@lstmed.ac.uk or First floor, Centre for Maternal and Newborn Health, Wolfson building, Liverpool School of Tropical Medicine, Pembroke place, L3 5QA, Liverpool.

Annex 4B: Participant Information Sheet: KII Participants

Early warning System to improve maternal health in Nigeria: *Design, validation and evaluation of modified obstetric early warning chart for use in resource limited settings*

INVITATION TO TAKE PART IN A RESEARCH STUDY INVITATION TO TAKE PART IN A RESEARCH STUDY

Good day Sir/Madam!

My name is Aminu Aliyu Umar, I am a first-year postgraduate research degree student at the Centre for Maternal and New-born Health, Liverpool School of Tropical Medicine, University of Liverpool. I am conducting this brief study as part of my PhD research entitled "*Early warning system to improve maternal health in Nigeria, design, validation and evaluation of modified obstetric early warning chart for use in resource limited settings'.* I hereby cordially invite you to take part in this study. However, it is important that you know why the research is being done, and what it entails before deciding to take part. Kindly take time to go through this document carefully, discuss it with family or friends if you wish, and you are free to decide whether to take part or not.

PURPOSE OF THE STUDY

The need for this study arose from the high prevalence of maternal deaths in the developing countries, and especially in Nigeria; out of the 303,000 maternal deaths that occurred around the world in 2015, approximately twenty percent were contributed by Nigeria alone. Many of these deaths have been attributed to delay in recognizing complications of pregnancy and childbirth.

A clinical tool (obstetric early warning chart) is capable of recognizing women who are likely to benefit from an earlier life-saving intervention. This tool has been in use in the hospitals and maternities in the United Kingdom and other developed countries for over a decade now. Use of this tool in monitoring sick pregnant and delivered women has been proven to reduce maternal deaths and number of women suffering irreversible complications related to pregnancy and childbirth significantly. Thus, the overall aim of my project is to introduce and evaluate the use of obstetric early warning system for maternal monitoring in Nigerian hospitals.

To look at feasibility and predict possible problems with implementation of obstetric early warning chart in Nigeria, it was deemed necessary to conduct an initial pilot feasibility study in selected hospitals; this stage is where the study is at the moment. In this phase, we intend to conduct an observation of maternal care/treatment monitoring practices, conduct key informant interviews targeting

senior midwives/nurses and, conduct focus group discussions with midwives who perform monitoring of pregnant or recently delivered women in maternity, obstetric wards/high dependency units.

What is an obstetric early warning system

These are systems designed, for use in all obstetric inpatients, to track maternal physiological parameters, and to aid early recognition and treatment of the acutely unwell parturient. They assign weighted values to a few parameters (often six vital signs in most of the charts), according to their degree of deviation from normal, and define a threshold beyond which mandatory actions must be taken to prevent irreversible complications or death. I have attached a copy of the Modified Obstetric Early Warning (MOEWS) chart that is in use in a hospital in the United Kingdom (Liverpool Women's hospital). Please note that we don't intend to adopt this for use in Nigeria, but just attached it to give you a clear view of how the early warning system works for the sake of the interview.

What is required of you

I will require you to participate in an interview, during which you will be answering questions on the following aspects of patient care; monitoring of vital signs and other aspects of clinical examination of patients in your place of work, monitoring of patients with different categories of obstetric complications, existing track and trigger system and finally your opinions on obstetric early warning systems. You have one week to decide whether to take part in this exercise. If you agree to participate, I will require you to sign an informed written consent before we commence the interview session.

TIME COMMITMENT

The interview will take approximately 30-45 minutes.

TERMINATION OF PARTICIPATION

Your participation in this study is absolutely voluntary, and you may decide to stop being a part of the study at any time without explanation and without penalty.

CONFIDENTIALITY/ANONYMITY

Please note that the following measures are going to be taken to ensure absolute anonymity and confidentiality in the conduct of the study.

- The data collected do not contain any personal information about you.

- No one will be able to link the data you provided to your identity and name.
- The data will be seen only by the researchers and will not be made available to anyone else.
- The audio recordings will be kept until the final report is completed, after which time they will be destroyed."

FOR FURTHER INFORMATION ABOUT THIS RESEARCH STUDY

I will be glad to answer your questions about this study at any time. You may contact me at aminu.umar@lstmed.ac.uk or First floor, Centre for Maternal and Newborn Health, Wolfson building, Liverpool School of Tropical Medicine, Pembroke place, L3 5QA, Liverpool.

Annex 4B: Participant Information Sheet: FGD Participants

Early warning System to improve maternal health in Nigeria: *Design, validation and evaluation of modified obstetric early warning chart for use in resource limited settings*

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What is required of you

I will require you to participate in a Focus Group discussion, during which you will be discussing the following aspects of patient care with your colleagues; monitoring of vital signs and other aspects of clinical examination of patients in your respective wards, monitoring of patients with different categories of obstetric complications, existing track and trigger system in your respective wards and finally your opinions on obstetric early warning systems. You have one week to decide whether to take part in this exercise. If you agree to participate, I will require you to sign an informed written consent before we commence the session.

TIME COMMITMENT

Each FGD will take about 45-75 minutes.

TERMINATION OF PARTICIPATION

Your participation in the Focus Group Discussion is absolutely voluntary, and you may decide to stop being a part of the study at any time without explanation and without penalty.

CONFIDENTIALITY/ANONYMITY

Please note that the following measures are going to be taken to ensure absolute anonymity and confidentiality in the conduct of the study.

- The data collected do not contain any personal information about you.
- No one will be able to link the data you provided to your identity and name.
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Annex 4C: KII and FGD Log

FGD/KII LOG

Background information

Thank you for participating in this exercise. There are only a few basic rules to keep in mind while participating today:

a) Everyone is expected to be an active participant.

b) There are no "right" or "wrong" answers.

c) Speak freely but remember not to interrupt others while they are talking.

d)

f) All feedback today will remain anonymous. To maintain anonymity, I just ask that anything that is said during our session is not repeated outside of our session.

g) Note taking is for reporting purposes only and will be used for analysis. Names are not attached to the notes. Kindly fill out the following details,

1) Exercise_____ (KII or FGD)

2) Date _____

3) Duration _____

Log

Participant's ID	Cadre	Rank	Ward	Years practicing	Years on the ward	*Clinical work	*Admin work

*state percentage of time of work spent performing each of the two activities

Annex 4D1: Topic guide for KII with nurses and midwives

1) CHARACTERISTICS OF THE PARTICIPANTS

Interviewer need to fill out the KII log before the start of interview

2) EXPLORING MATERNAL MONITORING PRACTICE

i) Can you please tell us what cadres of healthcare staff are responsible for undertaking the tasks of monitoring sick pregnant women, women in labour and recently delivered women in this facility?

PROMPT; task of vital signs monitoring, examinations including VE, variation of roles with staff rank

ii) We would like to hear about maternal monitoring in this facility – specifically we are interested in your job description with respect to monitoring of sick pregnant and recently delivered women. To start with, can you describe how these categories of patients are monitored?

PROMPT; How a woman in labour is monitored, sick pregnant woman, puerperal complications, women in HDU

PROBES; What vitals are monitored, frequency of monitoring

iii) Under what circumstances does the monitoring pattern changes per guidelines, and how does it change?

iv) Can you explain to us what abnormal findings from patient monitoring constitute a trigger (calls for alarm)?

PROMPT; from vital signs chart, from other aspects of patient monitoring

v) Please tell us how a healthcare staff undertaking patient monitoring should trigger a response to abnormal findings?

PROBES; is this different from what is done in day-to-day practice? How different, why different

vi) Can you please share your opinion about what the attitude of healthcare staff is like to maternal monitoring in this facility?

3) PERCEPTION ON OBSTETRIC EARLY WARNING SYSTEM (EWS)

Now we would like to hear your opinion about obstetric early warning system (discussed with interviewee prior to interview, and read about it on the information sheet).

i) First, how do you perceive the relevance of such a system to maternal care in this facility?

PROMPT; do you think it would be useful? why and how?

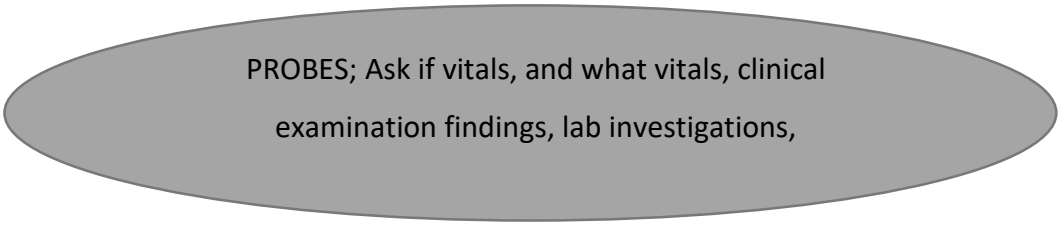
II) What potential challenges do you anticipate if a system like this is introduced?

III) How do you think these challenges can be addressed?

4) SUGGESTIONS REGARDING OBSTETRIC EARLY WARNING SYSTEM

Supposing we want to introduce EWS to alert you about maternal emergencies

i) What information would you expect to see on such a system?



ii) In your view, what form should the system take and why?

PROMPT; Paper based, software on the computer, android app on the phone

iii) What level of staff do you expect to be using it?

iv) What would you recommend to ensure adherence to use?

v) Would you like to add any comment?

Annex 4D2: Topic guide for KII with doctors

TOPIC GUIDE: KEY INFORMANT INTERVIEW WITH DOCTORS

CHARACTERISTICS OF THE PARTICIPANTS

No; _____ **Hospital** _____

Designation_____ **Duration of experience**_____

Q; When was the last time you had a call to review a patient?

Probe; Labour, Pregnancy complication, postpartum complication

Prompt; What case, from where, key information, listen for vitals, how was message conveyed,

Q; Among the information received, which part gave you an idea of the urgency of the situation?

Probe; what is perceived as relevant, what was irrelevant

Q; What factors in your opinion could affect how quickly you respond when called?

Probe; how it was communicated, what information; history, examination findings, vital signs

Prompt; which part of the information could have been improved to make you react more promptly?

A brief discussion on early warning chart and how it works

Q; Supposing there is evidence that this system helps in early detection of deterioration, how do you see it working in your setting?

Probe; feasible? Acceptability?

Prompts; Who should use the chart, wards

Q; Regarding the design, what information would you want the chart to have?

Probe; vital signs, other exam findings, labs,

Prompts; what form should it be, paper, soft in computer, android app

Q) In your view, what abnormality do you think should constitute a trigger?

Probe; cumulative scores, single parameter score

Q; Knowing your setting, what do you think could facilitate its working?

Probe; Challenges

Q; what additional information would you want to add to this interview?

Annex 4E: FGD topic guide

CHARACTERISTICS OF THE PARTICIPANTS

Interviewer need to fill out the FGD log before the start of interview

Based on your experience working in the labour, obstetric wards/high dependency units (HDU), what tasks are you expected to accomplish?

PROMPT; Labour ward staff, Obstetric wards staff, HDU/CCU staff to discuss roles separately without a particular order.

PROBES; ask if they do any of the following if not mentioned; monitoring women in labour, sick

Which tasks do you actually carry out in reality, and why?

PROBES; How much of your time do you spend on maternal monitoring compared to other tasks?

We would like to hear about how you conduct maternal monitoring – specifically we are interested in vital signs and their frequency of monitoring. Can you please describe how these tasks are undertaken in your respective wards?

PROMPT; How a woman in labour is monitored, sick pregnant woman, puerperal complications, women in HDU

PROBES; What vitals are monitored, frequency of monitoring

Is this different from the expected?

PROBES; How different? Why different?

Under what circumstances the above monitoring does patterns changes, and how does it change?

Can you explain to us what abnormal findings from patient monitoring constitute a trigger (calls for alarm)?

PROMPT; from vital signs chart, from other aspects of patient monitoring

Please tell us how a response to abnormal findings from patient monitoring is triggered?

PROBES; Ask how the staff responds to trigger,

who to call out, when to call, what does he/she

Now we would like to hear your opinion about obstetric early warning system (discussed with interviewee prior to interview and read about it on the information sheet).

First, how do you perceive the relevance of such a system to maternal care in this facility?

PROMPT; Do you think it would be useful? Why and how?

Supposing we want to introduce EWS to alert you about maternal emergencies

What information would you expect to see on such a system?

In your view, what form should the system take and why?

PROMPT; Paper based, software on the computer, android app on the phone

What would you recommend to ensure adherence to use?

What potential challenges do you anticipate if it were to be used in this facility?

What additional comment would you like to add?

Annex 4F1: Summary table of the sub-themes related to monitoring

Anchor code	**Maternal Monitoring**		
Theme	**Monitoring**		
Sub-themes	**F***	**Meaning**	**Evidence**
Who monitors	17	The staff that perform monitoring of women in labour, sick pregnant and postpartum women	*…we have the midwives, the nurses and sometimes the CHEWS due to man power problem… (KII B01)* *…It is the nurses and the doctors at times crosscheck… (KII A05)*
Hierarchy in monitoring	10	Variation of roles with staff rank and experience	*.. yes, there are variation of roles here… (KII B02)* *...everybody does but sometimes we try to prioritize some roles to the more experienced hands… (KII N02)*
Parameters monitored	15	What parameters are routinely monitored	***…****they are pulse, respiration, temperature and blood pressure and foetal heart rate (FGD A06, A02)* *…SPO2, Urinalysis, uterine contractions, VE and examination of the gravid uterus (observation, KII N03)*
Frequency in labour	19	Frequency of vital signs monitoring in women that are in labour	*…we do check the foetal heart rates every 30 minutes, and other vitals hourly if she is in active phase, if she is in latent phase then we do it four hourly… (FGD A02)* *…If she is in active phase, we do it every hour, but if she is in latent phase of labour, we do vitals every four hours... (FGD N02)*
Frequency in others	14	Frequency of monitoring vital signs	*…we monitor the vital signs of the patients once in every shift, if there is no complication. (FGD B05)* *…Routinely in this hospital vitals are taken twice for stable patients, in the mornings and evenings… (FGD N05)*

F*= Frequency. This is the number of references put into the sub-themes (nodes) in the NVivo

Annex 4F2: Summary table of the sub-themes related to circumstances affecting monitoring

Anchor code	Maternal monitoring		
Theme	Circumstances and how they affect monitoring		
Sub-themes	**F***	**Meaning**	**Evidence**
Maternal conditions	35	Clinical condition of the woman	*…in cases of preeclampsia, eclampsia or haemorrhage, you will need to monitor more frequently (FGD N03)* *…if labour is either augmented or induced we monitor the patient quarter hourly (N01)*
Foetal conditions	16	Clinical state of the foetus	*…If the foetal heart is less than 120 or above 160 we start monitoring closely, get the doctor informed and connect the patient to CTG (FGD A03)* *...in case of foetal distress, you give oxygen, you position the patient well, left lateral position, if she is likely to require surgery you prepare her while waiting for the doctors (FGD A05)*
Time of presentation	10	Time of presentation to the health facility	*…most of our patients usually come when the cervix is fully dilated unless those who be afraid of delivery (B01)* *…Late presentation keeps bothering us in this hospital... (FGD B05)*

F*= Frequency. This is the number of references put into the sub-themes (nodes) in the NVivo

Annex 4F3: Summary table of the sub-themes related to staff attitude

Anchor code	**Maternal monitoring**		
Theme	**Staff attitude**		
Sub-theme	**F***	**Meaning**	**Evidence**
Good	11	All staff have good attitude to monitoring and caregiving	*"…everybody is trying his best to ensure patients feel at home… (KII A* *"…I think our attitude toward monitoring is good… (KII N02)"*
Bad	2	The attitude of staff to work is not encouraging	*"…no things are just going down unlike before, that is just the fact… (KII B02)"* *"… she is confident because she has somebody up there, attitude to wok is just not encouraging… (KII B01)"*
Mixed	4	Some have a good attitude to work, while others' is bad.	*"…the staff are trying actually but when you are over stretched, it makes you to harass patients sometimes… (KII B01)"*

F*= Frequency. This is the number of references put into the sub-themes (nodes) in the NVivo

Annex 4F4: Summary table of the sub-themes related to track and trigger

Anchor code	**Maternal monitoring**		
Theme	**Track and trigger**		
Sub-theme	**F***	**Meaning**	**Evidence**
When to call	21	Conditions that requires intervention from doctors, also known as triggers	*"…they have mentioned the most important conditions that require help, such as haemorrhage, preeclampsia and eclampsia. Another condition is anaemia… (FGD A03)*
How to call	13	How a response from doctor is triggered in the facilities	*"…Since we are with them, we normally talk to them directly A03…"* *"…By phone, we use intercom and call them A01…"* *"…we send attendants to call them from their offices or clinics (FGD A01)"*
Who to call	10	Who is contacted when there is a trigger	*"We send for the doctors. They normally don't stay with us, but are not quite far from our reach… (FGD A01)"* *we don't call the house officers alone, we call the registrar (KII N03)*
Management of trigger	15	How midwives and nurses intervene while awaiting response from doctors	*"…while waiting for the doctors to turn up, we do our basic nursing interventions depending on the condition… (FGD A06)"*

F*= Frequency. This is the number of references put into the sub-themes (nodes) in the NVivo

Annex 4F5: Summary table of the themes related to perception and acceptability

Research question	**What is the perception of health workers on EWS and its acceptability?**		
Themes	**Perception and Acceptability**		
Sub-theme	**F***	**Meaning**	**Evidence**
		Perception	
Positive	25	Participants feel EWS is a good innovation and potentially very useful	*"…the idea is very much welcome and since we are looking forward to developing our medical practice to what is obtainable in the developed world, this is going to be a major step (FGD B06)"* *"…I think it is very useful and it will help in reducing maternal mortality rate, in our hospital… (KII N01)"*
Mixed	2	Participant feel EWS may be good, but has many downsides as well.	*"…for me it looks good, but you know people are always resistant to new things, so I really am not sure…(FGD A06)"*
Negative	1	Participants feel EWS is not a worthwhile innovation or is not potentially useful in their workplace	*"…it's just like the partograph that we use, so it may just be an additional paper work for us… (KII A02)"*
Acceptability			
Acceptable	15	Participants are ready to accept EWS if introduced, and are confident of its acceptability to other staff	*"…no, it's good, it's a good one, it's a welcome idea, we here are open to positive change, we want to move with the world (KII N03)"* *"I don't foresee any resistance from our staff here… (KII A05)"*
Unacceptable	1	Participants feel EWS may not be accepted for one reason or the other if introduced	*"…acceptance is an issue because I know some will definitely be against it… (KII N01)"*

F*= Frequency. This is the number of references put into the sub-themes (nodes) in the NVivo

Annex 4F6: Summary table of the themes related Challenges to EWS implementation

Research question	**What are the possible challenges to implementation of EWS in the feasibility study sites?**		
Themes	**Challenges and Way forward**		
Sub-themes	**F***	**Meaning**	**Evidence**
Man-power	14	Inadequate nurses and midwives and associated high workload in the hospitals	*"…To me is ok the only thing is that we don't have enough manpower here… (KII A03)"* *"…although we try our best to do the right thing, but sometimes the work can be overwhelming… (FGD N05)"*
Monitoring equipment	10	Faulty and or insufficient monitoring equipment in the hospitals	*"…like here we have only one BP machine on the ward… (FGD B03)"* *"…we need electronic monitoring machines. We need blood pressure machine, we need computers… (FGD N05)"*
Other challenges	5	Challenges other than man-power and equipment problem	*"… Provision of the tools too, sometimes continuity is an issue, you start something after short time, you find out there is no supply… (KII B02)"* *"…the stationaries are also not available just paper to write at times is a problem here… (KII B01)"*
Solutions	29	Measures to address the challenges and make implementation of the chart a success	*"…I will recommend training and retraining of healthcare personnel… (FGD N04)"* *"…on the man-power shortage, the government and NGOs should help. the management also has a big to play… (KII A01)"*

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Annex 4F7: Summary table of the themes related to challenges to EWS implementation

Theme	**Suggestion on EWS**		
Sub-themes	**F***	**Meaning**	**Evidence**
Design	17	Suggestions of participants regarding the design of the chart that is proposed to be used in their facilities	*"…we will prefer a paper, that we can use without shortage or power outage (FGD A04)"* *"…may be with time we might change but presently we are still using paper… (KII A01)"*
Parameters	24	Suggestions of participants regarding what parameters to include in the chart in view of the peculiarities of their setting	*"…For the vitals on the chart, we do pulse temperature, respiration, blood pressure and foetal heart rate all here. (FGD B03)"* *"…It should contain a score of pain and urine output too…as you know all these do not require equipment to do… (FGD N05)"*
Who to use	9	What level of staff do participants expect to use the chart if introduced	*"…the nurses, midwives and the doctors too especially the junior ones… (KII A01)"*

F*= Frequency. This is the number of references put into the sub-themes (nodes) in the NVivo

Annexes Chapter 5

Annex 5A: Propose score-based EWS monitoring chart

OBSTETRIC EARLY WARNING CHART

Name: ______________________ Hosp number: ___________ Ward: ______________________ Consultant: _____________ Diagnosis: ___________________ Gravidity/Parity:	For score of 0 or 1, repeat observations 12 hourly or as usual for post op patients For score of 2, repeat after 30 minutes, if it remains 2 or rises, inform Doctors For score of 3 or more, or if concerned regardless of score, please call doctors Doctors review time should be completed only for triggered patients

Date	Time		Temp	Pulse	RR	Sys BP	Urine vol	Cons level	Del mode	EWS	Review time	Sign
		Observation										
		Score										
		Observation										
		Score										
		Observation										
		Score										
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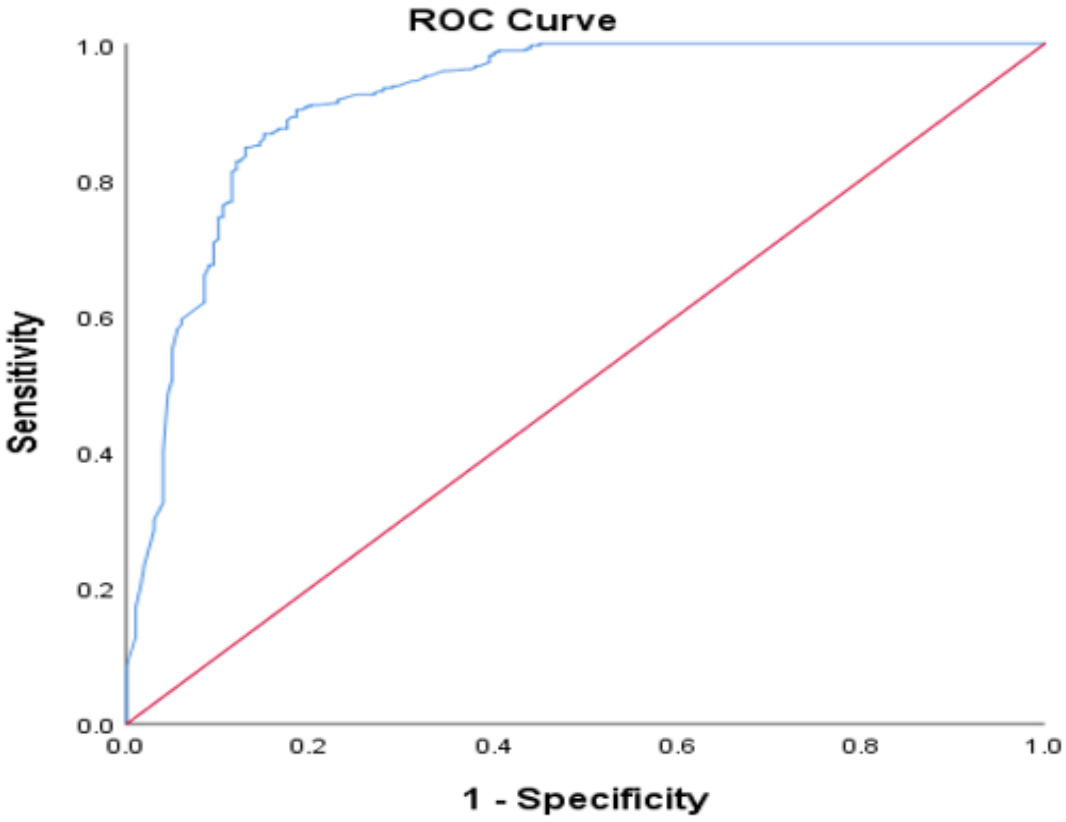
		Observation										
		Score										

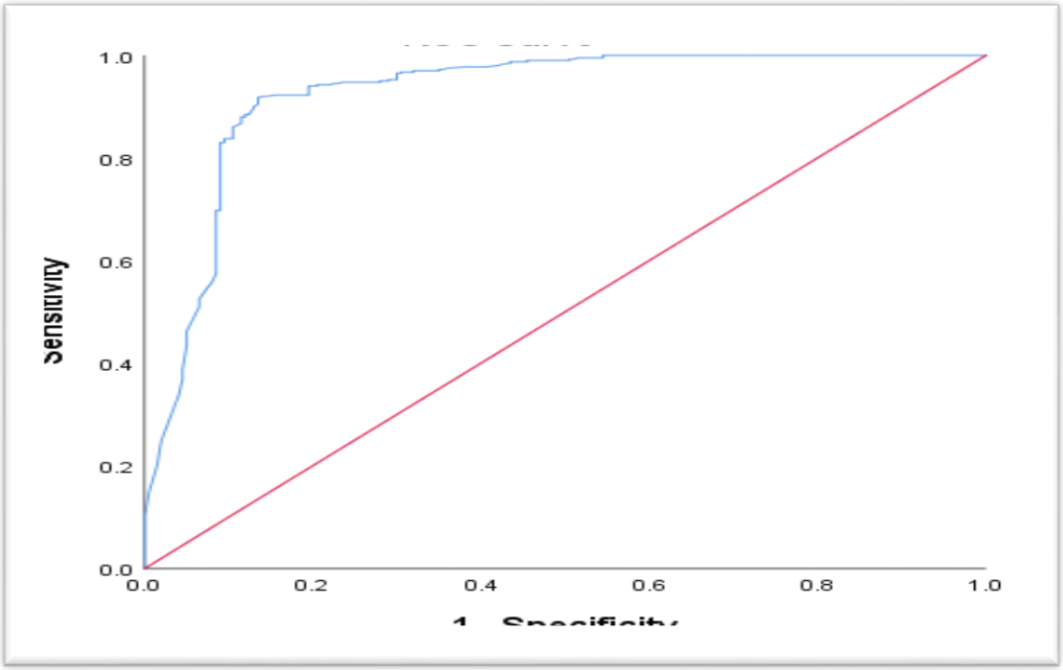
Score	**2**	**1**	**0**	**1**	**2**
Temperature	<35	35 – <36	36 – <38		>38
Pulse rate	<40	40 – <50	50 – <100	100 – 120	>120
Respiratory rate	0 – 10		11 – 20	21 – 30	>30
Systolic BP	<90	90 – <100	100 – <150	150 – 160	>160

Score	**0**	**1**	**2**
Urine (ml/hr)	>30	20 – 30	<20
Conscious level (AVPU)	Alert	Response to voice	Response to pain/unresponsive
Delivery mode	SVD	C/S	

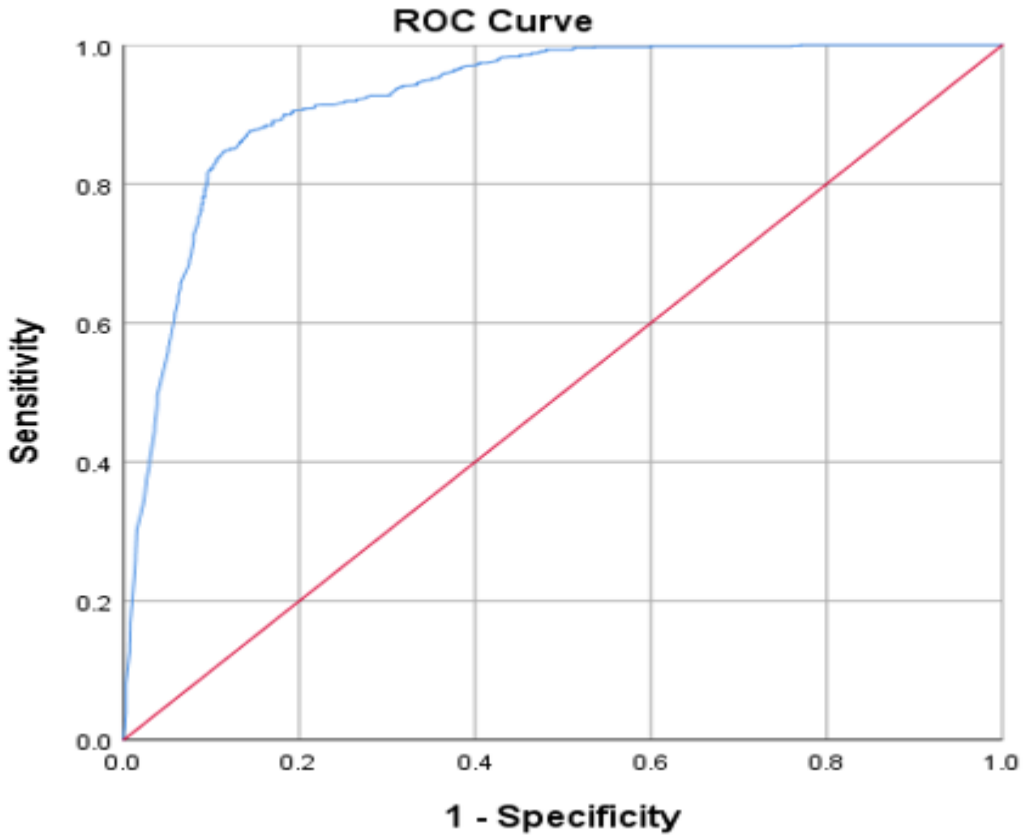
Annex 5B: ROC Analysis derivation model



Annex 5C: ROC Validation model 1 (n=600)



Annex 5D: ROC Validation model 2 (n=5243)



Chapter 6 Annexes

Annex 6A: EWS Chart

UITH OBSTETRIC EARLY WARNING CHART

Name: _____ Hosp number: _____

Ward: _____ Consultant: _____

For score of 0 or 1, repeat observations 12 hourly or as usual for post op patients
For score of 2, repeat after 30 minutes, if it remains 2 or rises, inform Doctors
For score of 3 or more, call doctors
If concerned, regardless of the score, please notify doctors

Date	Time		Temp	Pulse	RR	Sys BP	Dias BP	Cons level	Del mode	Total EWS	Signature
		Observation									
		Score									
		Observation									
		Score									
		Observation									
		Score									
		Observation									
		Score									
		Observation									
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		Score									
		Observation									
		Score									
		Observation									
		Score									
		Observation									
		Score									

Score	2	1	0	1	2
Temperature	<35	35 – <36	36 – <38		>38
Pulse rate	<40	40 – <50	50 – <100	100 – 120	>120
Respiratory rate	0 – 10		11 – 20	21 – 30	>30
Systolic BP	<90	90 – <100	100 – <150	150 – 160	>160

Score	0	1	2
Diastolic BP	<90	90 – 100	>100
Conscious level (AVPU)	Alert	Response to voice	Response to pain/unresponsive
Delivery mode	SVD	C/S	

Annex 6B: Trial data abstraction sheet

Annex 6B: TRIAL DATA ABSTRACTION SHEET
Testing effectiveness of obstetric early warning charts in improving measured outcomes

Month: _____ Year: _____

Total number of admissions/inpatients: _____

Number of research eligible patients reviewed: _____

Baseline characteristics

1. Mean (Q1-Q3)
   - Age _____
   - Weight _____
   - Height _____
   - Booking GA _____
   - Parity _____
   - GA at delivery _____
   - Number ANC visit_____

2. Number (%)
   - Booked cases_____
   -Live birth _____
   -Still birth _____
   -Spontaneous abortion _____
   -Induced abortion _____
   -Birth weight _____

Primary outcomes

3. Number of maternal deaths_____ 4. ICU Admissions_____ 5. Near-misses _____

Condition	ICU/HDU Admission	Near-miss	Death	Total
Obstetric haemorrhage				
Pregnancy related infections				
Hypertensive disorders				
Prolonged labour				
Obstructed labour				
Thromboembolism				
Abortion complications				
Others, please specify _____				

Secondary outcomes

6. Rate of vital signs recording = (charts with completed vital sign / charts reviewed) in %
- Respiratory rate _____
- Pulse rate _____
-Systolic Blood pressure _____
-Diastolic blood pressure _____
-Temperature _____

7. Mean (Q1-Q3) duration of hospital stay in days _____

8. Mean (Q1-Q3) time interval between trigger and specialist review in minutes _____

9. Number (%) elective caesarean section
_____

10. Number (%) elective caesarean section
_____

11. Number (%) of instrumental deliveries
- Forceps _____
- Vacuum _____
-Destructive delivery _____
-Others _____

Annex 6C1: Phase 3 Key Informant Interview Topic Guide

CHARACTERISTICS OF THE INTERVIEWEE

ID No _____ Hospital _____

Designation_____ Duration of experience_____

Interviewer: The principal researcher will be responsible for coordination of the discussion, audio-recording and making notes, including context of the discussion. He is also responsible for general logistics and planning of all sessions.

Introduction

Thank you very much for sparing time to partake in this interview. We are meeting to discuss your experience in relation to obstetric early warning chart which was introduced to this facility some time ago. What we discuss here will remain confidential. I will start by asking you to identify and describe your role(s) regarding monitoring and care of obstetric inpatients. I will continue by asking what you feel are the advantages and downsides of the intervention, and what is your perception of its net usefulness in patient monitoring and care. If you happen to be one of the staffs using the chart for monitoring (nurse or midwife), Then I would ask you to describe very briefly some of the challenges experienced after implementation of the tool. I will then go on to ask about some of these challenges in more details and review your opinion on how they were (or can be) surmounted. The entire session will take about 45 minutes. I will audio-record the sessions but nothing you said will be linked to you during or after analysis.

Specific interview questions

1. Can you please describe your role (s) in regards to monitoring and care of obstetric inpatients admitted to all hospital wards (or ICU as the case may be).

   Probe: ask for general roles, link to the early warning chart use, or response to trigger (as appropriate)

   If the interviewee does not use the chart primarily for patient monitoring (is a doctor), skip 2 and 3.
2. Can you please describe your experience of the use of obstetric early warning chart?

Probe; ease of use, compare to earlier practice, accuracy in identifying deterioration

3. What challenges did you encounter while using the obstetric early warning chart?

   Probe: Ask in depth and explore specific challenges

4. What, from your experience, do you consider as advantages of the obstetric early warning charts

   Probe: Ask in depth and explore specific advantages

5. What, from your experience, do you consider as the downsides of using obstetric early warning charts?

   Probe: Ask in depth and explore specific disadvantages

6. What is your perception of the net usefulness of obstetric early warning charts?

   Probe: Ask how participant will prioritize merits and demerits? which ones do you think outweighs the other?

7. Do you think the disadvantages can be remedied? if yes, what measures in your opinion can be taken to address them?

   Probe: Explore measures taken (that can be taken) to address each challenge (disadvantage) mentioned in 5 above.

8. How sustainable do you think this intervention (obstetric early warning chart) can be in this facility?

   Probe: Ask how long interviewee thinks adherence to use of the chart can last for, ask what factors can affect sustainability, explore factors/reasons

9. How do you think sustainability can be improved?

   Probe: Ask what measures can be taken to address factors mentioned in 8, ask what could have been done differently, how can the implementation program be improved.

10. Is there anything that you think is important and can add to this discussion?

Annex 6C2: Phase 3 Focus Group Discussion Topic Guide

CHARACTERISTICS OF PARTICIPANTS WILL BE COLLECTED IN THE FOCUS GROUP DISCUSSION LOG

Moderator: The principal researcher is responsible for coordination of the discussion
Assistant: A research assistant will be responsible for audio-recording and making notes, including context of the discussion. He is also responsible for general logistics and planning of all sessions.

Introduction

Thank you all for agreeing and sparing time to partake in this exercise. We are meeting to discuss your experience in relation to obstetric early warning chart which was introduced to this facility 3 month ago, as part of the emergency obstetric care training by the Centre for Maternal and Newborn Health, Liverpool School of Tropical Medicine. What we discuss here will remain confidential. I will start by asking you to identify and describe your role(s) regarding monitoring and care of obstetric inpatients. I will then ask you to discuss exhaustively your experience of patient monitoring with early warning chart and how that was different from the earlier practice of vital signs monitoring on nurses' chart. I will continue by asking what you feel are the advantages and downsides of the intervention, and what is your perception of its net usefulness in patient monitoring and care. This session will take about one hour. As you would have consented, I will audio-record the sessions to have accurate findings but can assure you that nothing you said will be linked to you during or after analysis.

Can we set our ground rules to foster good discussions?

Questions to be discussed

1. Can you please describe your role (s) in regard to monitoring and care of obstetric inpatients admitted to all hospital wards (or ICU as the case may be)?

   Probe: ask for general roles, link to the early warning chart use and triggering response based on the chart
2. Can you describe your experience of patient monitoring using obstetric early warning chart?

   Probe; ease of use, compare to earlier practice, accuracy in identifying deterioration

3. What do you consider as positive outcomes of implementing obstetric early warning chart on you or your practice?
4. What do you consider as Negative outcomes of implementing obstetric early warning chart on you or your practice?
5. On the piece of paper in front of you, jot down four of these items that you consider most important, separating the positives from negatives (two each).
   Probe: Collect the sheet and guide discussion using identified factors as guides
6. What is your perception of the net usefulness of obstetric early warning charts?
   Probe: Ask how you will prioritize merits and demerits, which ones do you think outweighs the other
7. Do you think the aforementioned negative outcomes can be remedied? if yes, what measures in your opinion can be taken to address them?
   Probe: Explore measures taken (that can be taken) to address each outcome (disadvantage) mentioned in 5 above
8. How sustainable do you think this intervention (obstetric early warning chart) can be in this facility?
   Probe: Ask how long participants thinks adherence to use of the chart can last for, ask what factors can affect sustainability, explore factors/reasons
9. How do you think sustainability can be improved?
   Probe: Ask what measures can be taken to address factors mentioned in 8, ask what could have been done differently, how can the implementation program be improved.
10. Is there anything that you think is important and can add to this discussion?

Annex 6D1: Phase 3 KII informed consent and information sheet

Name of Principal Researcher: Dr Aminu Aliyu Umar
Name of Organisation: Liverpool School of Tropical Medicine
Scoping activity: Key Informant Interview

This informed consent form has two parts:

• Information Sheet (to share information about the research with you)

• Certificate of Consent (for signatures if you agree to take part)

INFORMATION SHEET

BACKGROUND

You are invited to participate in this research project, which is part of a doctoral thesis, which is aimed at improving maternal and newborn outcomes through early detection of features of maternal deterioration with the aid of obstetric early warning chart. Before you decide, it is important for you to understand why the research is being done and what it entails. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you want more information. Take time to decide whether to participate.

You were chosen because you meet certain criteria for participation, which are: you provide care to (doctors), and or undertake monitoring of, women in labour, sick pregnant and recently delivered women (within puerperium) and might have been using the recently introduced obstetric early warning chart.

Ethical approval for this research was received from the research and ethics committee of the Liverpool School of Tropical Medicine and the Ethics and Research Committee of the University of Ilorin Teaching Hospital.

PURPOSE OF THE RESEARCH

The research is being conducted to understand the impact of the obstetric early warning chart on obstetric outcomes in the UITH and explore its usefulness among healthcare staff. The intervention was implemented as part of the EmONC training by the Centre for Maternal and Newborn Health, Liverpool School of Tropical Medicine. We want to understand how useful this tool has been, the challenges that might have been encountered while using it, and how best to address these challenges to ensure sustainability and improve quality of care given to women who are the ultimate beneficiaries.

PROCEDURE

You are being invited to take part in an interview. For this interview, the principal researcher (myself) will be guiding the discussion. Questions that you might have about the research can be answered at this point.

I will start by asking you to identify and describe your role(s) regarding monitoring and care of obstetric inpatients. I will continue by asking what you feel are the advantages and downsides of the intervention, and what is your perception of its net usefulness in patient monitoring and care. If you happen to be one of the staffs using the chart for monitoring (nurse or midwife), Then I would ask you to describe very briefly some of the challenges experienced after implementation of the tool. I will then go on to ask about some of these challenges in more details and review your opinion on how they were (or can be) surmounted.

The interview session will take place in [location of the interview], and no one else but myself and you will be present. The entire session will be recorded, with your permission, but no identifying information will be collected on the recording. Recordings will be stored on a secure drive and will be in possession of the principal researcher only. Information recorded is confidential. The recordings will be destroyed after 5 years.

DURATION

The interview session will be held once and will last about 45 minutes.

RISKS

There is a risk that you may feel uncomfortable talking about some of the topics. However, we do not wish for this to happen. You do not have to answer any question or take part in the interview if you feel the question(s) are too personal or if talking about them makes you uncomfortable.

POTENTIAL IMPACT ON PARTICIPANTS

There is no potential risk or discomfort in this research.

EXPECTED BENEFITS FOR PARTICIPANTS AND SOCIETY

By participating, you would be contributing invaluable feedback to be used in improving emergency obstetric care provision. There is no direct benefit to participant.

REIMBURSEMENTS

There will be no financial incentives to participants.

CONFIDENTIALITY

We will ask each of you to keep what was said in this session confidential. Any information obtained from you will be anonymised. All data will be entered into the database and securely stored. Data will be transported out of the country for analysis in the United Kingdom. Data will only be used for the purposes of this research.

DISSEMINATION OF RESULTS

Results will be published in peer-reviewed journals and in print and e-thesis format.

PARTICIPATION AND WITHDRAWAL

Choice to participate in this study relies solely on you. At any time during the research, you can choose to withdraw without consequence to you. You can refuse to answer any question you do not want to answer and still be part of the study.

RIGHTS OF PARTICIPANTS

You do not lose legal rights while participating in this study.

CONTACT

Please contact the principal researcher on the email address aminu.umar@lstmed.ac.uk , if you have questions or concerns about this study, or by mail to the undermentioned address.

Dr Aminu Umar

First Floor Wolfson building

Centre for Maternal and Newborn Health

Liverpool School of Tropical Medicine

Pembroke Place, L3 5QA, Liverpool, UK

+441517029389

CERTIFICATE OF CONSENT

The above information was clearly explained to me in English by the administrator of the instrument and I understand the language. I was given the opportunity to ask questions which were answered satisfactorily.

I hereby voluntarily consent to participate and have received a copy of this form.

I am also aware that the discussion will be recorded, and I consent to this.

_____

Signature of participant / Date

For administrator,

I certify that all information concerning the research was accurately provided to the participant.

_____

Signature of administrator / Date

A copy of this information will be given when you return the completed form.

THANK YOU

Annex 6D2: Phase 3 informed consent and information sheet (FGD)

Name of Principal Researcher: Dr Aminu Aliyu Umar

Name of Organisation: Liverpool School of Tropical Medicine

Scoping activity: Focus Group Discussion

This informed consent form has two parts:

• Information Sheet (to share information about the research with you)

• Certificate of Consent (for signatures if you agree to take part)

INFORMATION SHEET

BACKGROUND

You are invited to participate in this research project, which is part of a doctoral thesis, which is aimed at improving maternal and newborn outcomes through early detection of features of maternal deterioration with the aid of obstetric early warning chart. Before you decide, it is important for you to understand why the research is being done and what it entails. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you want more information. Take time to decide whether to participate.

You were chosen because you meet certain criteria for participation, which are: you provide the care to, and undertake monitoring of, women in labour, sick pregnant and recently delivered women (within puerperium) and have been using the recently introduced obstetric early warning chart in the course of discharging your clinical duties.

Ethical approval for this research was received from the research and ethics committee of the Liverpool School of Tropical Medicine and the Ethics and Research Committee of the University of Ilorin Teaching Hospital.

PURPOSE OF THE RESEARCH

The research is being conducted to understand the impact of the obstetric early warning chart on obstetric outcomes in the UITH and explore its usefulness among healthcare staff. The intervention was implemented as part of the EmONC training by the Centre for Maternal and Newborn Health, Liverpool School of Tropical Medicine. We want to understand how useful this tool has been, the challenges that might have been encountered while using it, and how best to address these

challenges to ensure sustainability and improve quality of care given to women who are the ultimate beneficiaries.

PROCEDURE

You are being invited to take part in a discussion with 5-7 other persons with similar backgrounds. For the focus group discussion, a member of the research team will guide the discussion. The focus group will start with the focus group moderator, making sure that you are comfortable. Questions that you might have about the research can be answered at this point.

We will start by asking you to identify and describe your role(s) regarding monitoring and care of obstetric inpatients. We will then ask you to discuss exhaustively your experience of patient monitoring with early warning chart and how that was different from the earlier practice of vital signs monitoring on nurses' chart. We will continue by asking what you feel are the advantages and downsides of the intervention, and what is your perception of its net usefulness in patient monitoring and care.

The discussion will take place in [location of the FGD], and no one else but the people who take part in the discussion, the note taker and I will be present. The entire discussion will be recorded, with your permission, but no one will be identified by name on the recording. Recordings will be stored on a secure drive and will be in possession of the principal researcher only. Information recorded is confidential. The recordings will be destroyed after 5 years.

DURATION

The focus group discussion will be held once and will last about one hour.

RISKS

There is a risk that you may feel uncomfortable talking about some of the topics. However, we do not wish for this to happen. You do not have to answer any question or take part in the discussion if you feel the question(s) are too personal or if talking about them makes you uncomfortable.

POTENTIAL IMPACT ON PARTICIPANTS

There is no potential risk or discomfort in this research.

EXPECTED BENEFITS FOR PARTICIPANTS AND SOCIETY

By participating, you would be contributing invaluable feedback to be used in improving emergency obstetric care provision. There is no direct benefit to participant.

REIMBURSEMENTS

Light refreshments will be provided during the focus group sessions, but there will be no financial incentives to participants.

CONFIDENTIALITY

We will ask each of you to keep what was said in the group confidential. You should know, however, that we cannot prevent participants who were in the group from sharing things that should be confidential.

Any information obtained from you during the discussion will be anonymised. All data will be entered into the database and securely stored. Data will be transported out of the country for analysis in the United Kingdom. Data will only be used for the purposes of this research.

DISSEMINATION OF RESULTS

Results will be published in peer-reviewed journals and in print and e-thesis format.

PARTICIPATION AND WITHDRAWAL

Choice to participate in this study relies solely on you. At any time during the research, you can choose to withdraw without consequence to you. You can refuse to answer any question you do not want to answer and still be part of the study.

RIGHTS OF PARTICIPANTS

You do not lose legal rights while participating in this study.

CONTACT

Please contact the principal researcher on the email address aminu.umar@lstmed.ac.uk , if you have questions or concerns about this study, or by mail to the undermentioned address.

Dr Aminu Umar
First Floor Wolfson building
Centre for Maternal and Newborn Health
Liverpool School of Tropical Medicine
Pembroke Place, L3 5QA, Liverpool, UK
+441517029389

CERTIFICATE OF CONSENT

The above information was clearly explained to me in English by the administrator of the instrument and I understand the language. I was given the opportunity to ask questions which were answered satisfactorily.

I hereby voluntarily consent to participate and have received a copy of this form.

I am also aware that the discussion will be recorded, and I consent to this.

_____

Signature of participant / Date

For administrator,

I certify that all information concerning the research was accurately provided to the participant.

_____

Signature of administrator / Date

A copy of this information will be given when you return the completed form.

THANK YOU

Annex 6E: phase 3 trial quality assessment checklist

Day and Month: _____ Year: _____

1. Total number of admissions/inpatients: _____
2. Number of research eligible patients reviewed: _____
3. Number of patients in 2 above with correctly completed obstetric early warning chart: _____
4. Compute the usage rate of Obstetric early warning chart: _____

   NB

   Usage rate = (result of number 3 / results of number 2 above) expressed in %
5. Total number of charts requiring action based on the escalation guideline: _____
6. Number of cases in which action was taken: _____
7. Number of cases in whom action was required: _____
8. Compute an index (X) of whether healthcare staff took appropriate action to abnormal observation: _____

   NB

   X = (Findings in number 6 / Findings in number 7) expressed in %
9. Number of triggered patients in whom review was done within one hour of trigger _____
10. Compute index of timeliness of action taken (Y): _____

NB

Y = total number where action was taken within the required timeframe/total number where action was taken

Y = (Findings in 9 / findings in 6 above)

Annex 8: Systematic review paper

Annex 9: Design and validation manuscript

ARTICLE ID														
Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**Article Title**	**1. Author(s)**	**2. Year of publication**	**3. Type of publication (e.g. commentary, systematic**	**4. Year(s) of study (year(s), not clear, not stated, not applicable)**	**5. Country/ies of study (country/ies, not clear, not**	**6. Level of care (indicate facility/ies type(s)—tertiary health facility, secondary health**	**7. Objective/purpose of paper**	**8. Study design (if applicable)**	**9. Participants and characteristics (Indicate sample size and a brief description of the participants eg pregnant, postpartum, or in critical care)**	**9a. Comment on 9 (if any)**
SR40	AAU	AAU	FMU	Use of Maternal Early Warning Trigger tool reduces maternal morbidity	Laurence E. Shields,	2016	Original rsearch	Oct 2014-Oct 2015 (13)	USA	29 Facilities; No information to discern level	to prospectively evaluate the use of a pathway-specific Maternal Early Warning Trigger (MEWT) tool and determine if its use was associated with a reduction in maternal morbidity.	Non randomized trial	Obstetric admissions to 6 pilot sites (n=11,399)	There was no clear inclussion criteria for MEWT intervention participants at the pilot sites
SR22	AAU	AAU	FMU	Performance of the Obstetric Early Warning Score in critically ill patients for the prediction of maternal death.	Angel Paternina-Caicedo	2017	Original rsearch	Jan 2006-Dec 2011	Columbia	Tertiary referral centre	to assess the performance of the Intensive Care National Audit and research Center Obstetric Early Warning Score in predicting death among pregnant women who required admission to the intensive care unit.	Retrospective cohort study (single centre)	Pregnant and postpartum women (upto 42 days) admitted into the ICU (n=702)	Participants included direct and indirect obstetric admissions; direct obstetric -related disorders were deffined as those resulting from obstetric complications of the pregnant state (pregnancy, delivery and postpartum) or chain of events resulting from pregnancy-related disorders (hypertensive disorders in preg- nancy). Indirect obstetric causes were defined as those resulting from preexising conditions or conditions that developed during pregnancy and may have been aggravated by physiologic effects of pregnancy, but were not due to direct obstetric causes.
SR69	AAU	AAU	FMU	Evaluation of maternal early obstetric warning system (MEOWS chart) as a predictor of obstetric morbidity: a prospective observational study	Anju Singh	2016	Original rsearch	October 2012 to April 2014	India	Tertiary referral centre	to evaluate MEOWS chart as a bedside screening tool for predicting obstetric morbidity and to correlate each physiological parameter individually with obstetric morbidity	a prospective observational study	A total of 1065 woman which included pregnant women in labour beyond 28 weeks gestation and up to 6 weeks postpartum	All consecutive admissions to clean and septic labour wards were recruited into study depending
SR5	AAU	AAU	FMU	Maternal bacteraemia and the Irish maternity early warning system	Patrick J. Maguire	2015	Original rsearch	January 2009 to March 2013 (retrospective) and April 2013 to March 2014 (Prospectively)	Ireland	tertiary	to assess whether the introduction of IMEWS has improved the recording of vital signs among women with proven maternal bacteremia at the CWIUH	mixed retrospective and prospective study	all cases of maternal bacteraemia at CWIUH, Dublin, Ireland, between January 1, 2009, and 31 March 2014 (n=61 before and 20 after introduction of EWS)	Diagnosis of bacteraemia was based on the finding of bacterial growth on blood culture. Samples that were probably contaminated (according to laboratory protocol) were excluded

ARTICLE ID													
Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**Article Title**	**1. Author(s)**	**2. Year of publication**	**3. Type of publication (e.g. commentary, systematic**	**4. Year(s) of study (year(s), not clear, not stated, not applicable)**	**5. Country/ies of study (country/ies, not clear, not**	**6. Level of care (indicate facility/ies type(s)—tertiary health facility, secondary health**	**7. Objective/purpose of paper**	**8. Study design (if applicable)**	**9. Participants and characteristics (Indicate sample size and a brief description of the participants eg pregnant, postpartum, or in critical care)**	**9a. Comment on 9 (if any)**
SR10	AAU	AAU	FMU	Design and internal validation of an obstetric early warning score:secondary analysis of the Intensive Care National Audit and Research Centre Case Mix Programme database	Carle C	2013	Original rsearch	Dec 1995-Sep 2008	UK	Tertiary	to design and then internally validate a statistically based aggregate weighted EWS specific to the obstetric population	retrospective analysis of secondary data	Females aged 16-50 (n=71108) categorized into direct obstetric, indirect obstetric and non obstetric admission groups. 4440 direct obstetric admissions were the study participants.	Model development set consist of 2240 randomly assigned direct obstetric admissions and validation set consist of 2200 direct obstetric admissions
SR61	AAU	AAU	FMU	A validation study of the CEMACH recommended modified early obstetric warning system (MEOWS)	Singh S	2012	Original research	Not stated, but data collected for 2 months	United Kingdom	tertiary referral hospital	The aim of our study was to evaluate the MEOWS as a tool for predicting maternal morbidity, by measuring its sensitivity, specificity and predictive value	prospective observational study	All women between 20 weeks' gestation and 6 weeks postpartum, who were admitted as an inpatient to the maternity unit, were included in the study (n=676)	NA
SR33	AAU	AAU	FMU	Baseline assessment of a hospital-specific early warning trigger system for reducing maternal morbidity	Hedriana	2016	Original research	July 2012-May 2013	USA	7 pilot hospitals in dignity health- 29 of the 38 hospitals in dignity health provide primary to tertiary maternity services.	to investigate whether predetermined maternal early warning triggers (MEWTs) can be used to predict an escalating state of morbidity as a first step to reduce maternal morbidity and mortality	retrospective case–control study	n=50 cases and 50 controls. Eligible patients in the case group were at term or preterm with vaginal bleeding, hypertension, abdominal pain, labour, ruptured membranes, fever, gastrointestinal symptoms, and other symptoms requiring evaluation in obstetric triage, were consequently admitted for treatment, and were subsequently transferred to the ICU from the peripartum, intrapartum, and postpartum units. An equal number of patients admitted to the maternity units after triage with normal delivery outcome over a 24-hour period formed the control group	The exclusion criteria were direct admission to the ICU from the emergency department or the operating room, and transferal from other facilities

ARTICLE ID														
Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**Article Title**	**1. Author(s)**	**2. Year of publication**	**3. Type of publication (e.g. commentary, systematic**	**4. Year(s) of study (year(s), not clear, not stated, not applicable)**	**5. Country/ies of study (country/ies, not clear, not**	**6. Level of care (indicate facility/ies type(s)—tertiary health facility, secondary health**	**7. Objective/purpose of paper**	**8. Study design (if applicable)**	**9. Participants and characteristics (Indicate sample size and a brief description of the participants eg pregnant, postpartum, or in critical care)**	**9a. Comment on 9 (if any)**
SR62	AAU	AAU	FMU	Validating the Performance of the Modified Early Obstetric Warning System Multivariable Model to Predict Maternal Intensive Care Unit Admission	Helen M. Ryan	2017	Original research	January 1 2000 to 31 December 2011	Canada	Two tertiary obstetric hospitals	The aim of this study was to externally validate the current CEMACH MEOWS tool using Canadian data for pregnant and recently pregnant, hospitalised women and to assess for the possibility of developing a multivariable tool based on the current MEOWS tool	Retrospective, observational, case-control validation study	46 cases and 138 controls; Cases included pregnant or recently pregnant (<6 weeks after the end of the pregnancy, irrespective of gestational age at the end of the pregnancy) admitted women who subsequently required admission to the ICU for >24 hours. Control patients were the first three women identified from hospital databases who were either pregnant or recently pregnant and admitted to the hospital for >24 hours during that time who did not receive critical care, matching for year of admission but for neither antenatal nor postpartum state of cases at the time of ICU admission.	Because these were the limits of the data available, no formal sample size calculation was performed.
SR44	AAU	AAU	FMU	Implementation of warning tool to improve maternal newborn health outcomes in a developing country	Sana Sheikh	2017	Original research	April to July 2014	Karachi, Pakistan	38-bed secondary-care facility	to improve maternal and perinatal outcomes through implementation of NEWS for themanagement of obstetrics patients during off-work hours, i.e., from 1700 hours to 0800 hours, in a secondary-level hospital	Before after study design	200 women who had emergency caesarean section during off work hours, 100 each in group A and B. Patients who had CS before the implementation of NEWS constituted Group A and those who had it after the implementation constituted Group B	Offwork hours were selected because even in hospitals with high standard of care, quality of care gets affected during these hours because of limited human resources and clinical experts.
SR35	AAU	AAU	FMU	Modified obstetric early warning scoring systems (MOEWS): validating the diagnostic performance for severe sepsis in women with chorioamnionitis	Sian E. Edwards	Apr-15	Original research	June 2006 through November 2007	Chicago, USA	Tertiary referral centre	The aim of this study was to compare the predictive power of MOEWS in women with chorioamnionitis.	retrospective cohort study using prospectively collected clinical observations	913 women with chorioamnionitis, defined clinically as maternal pyrexia in labour (38C) associated with uterine tenderness, maternal or Fetal tachycardia, or purulent/ foul-smelling amniotic fluid	There were no specific exclusion criteria
SR40	AAU	AAU	FMU	High dependency unit admissions during the first year of a national obstetric early warning system	Patrick J. Maguire	2015	Original research	April 1, 2013 and March 31, 2014	Ireland	Tertiary referral centre	The present observational study evaluated the first year of prospective implementation of the IMEWS in the Coombe Women and Infants University Hospital, a tertiary center	Retrospective observational study of prospectively collected data	Women admitted to ICU in the first year of prospective implementation of the IMEWS. IMEWS had been used for 80 (47.9%) patients before HDU admission, with other monitoring methods employed for 87 individuals (52.1%, excluded in this analysis)	NA

ARTICLE ID													
Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**Article Title**	**1. Author(s)**	**2. Year of publication**	**3. Type of publication (e.g. commentary, systematic**	**4. Year(s) of study (year(s), not clear, not stated, not applicable)**	**5. Country/ies of study (country/ies, not clear, not**	**6. Level of care (indicate facility/ies type(s)—tertiary health facility, secondary health**	**7. Objective/purpose of paper**	**8. Study design (if applicable)**	**9. Participants and characteristics (Indicate sample size and a brief description of the participants eg pregnant, postpartum, or in critical care)**	**9a. Comment on 9 (if any)**
SR26	AAU	AAU	FMU	Existing models fail to predict sepsis in an obstetric population with intrauterine infection	Justin R. Lappen	2010	Original research	June 2006-November 2007	Chicago, USA	Tertiary	We examined SIRS and MEWS among pregnant women with intrauterine nfection and assessed whether these prognostic tools accurately predicted clinical decompensation.	retrospective analysis of patients with chorioamnionitis	All patients who were determined to have chorioamnionitis (n=913) were included in the study. Chorioamnionitis was defined as maternal fever in labor to at least 100.4°F with associated uterine tenderness, maternal or fetal tachycardia, or purulent or foul-smelling amniotic fluid	NA
SR55	FMU	FMU	AAU	Implementation of a modified obstetric early warning system to improve quality of Obstetric care in Zimbabwe.	Abi Merriel et al.	2017	Original research	April 2013 to January 2014	Zimbabwe	Mpilo Central Hospital, Bulawayo Zimbabwe - a government referral hospital	To implement a modified obstetric early warning system (MOEWS) to promote identification and stabilisation of unwell women.	Quasi experimental before and after study with a longitudinal "spot-check" study.	Women undergoing caesarean section before (n=79) and after (n=85)	none
SR70	FMU	FMU	AAU	Early detection of severe maternal morbidity: A retrospective assessment of the role of an early warning score system.	Diana M. Austin	2013	Original research	January 2010 to December 2011	New Zealand	Tertiary Hospital (Auckland City)	To determine whether EWS may have improved the detection of severe maternal morbidity or lessened the severity of illness among women with severe morbidity.	Application of an EWS to a restrospective and prospective cohort of pregnant and post-partum women admitted to ICU , CVICU and Obstetric HDU and	42 restrospective admissions and 71 prospective admissions	none
SR266	AAU	AAU	FMU	Prediction of adverse maternal outcomes in pre-eclampsia: development and validation of the fullPIERS model	Peter von Dadelszen	2011	Original research	Sept 1, 2003, and Jan 31, 2010	Canada, New Zealand, Australia, and the UK	academic tertiary obstetric centres	we aimed to develop and internally validate a pre-eclampsia outcome prediction model—the fullPIERS (Preeclampsia Intergrated Estimate of RiSk) model. fullPIERS was designed for use in well resourced settings.	prospective, multicentre cohort study	Women who were admitted to tertiary obstetric centres with pre-eclampsia or who developed pre-eclampsia after admission	Women were excluded if they were either admitted in spontaneous labour or had achieved any component of the maternal outcome before either fulfilling eligibility criteria or collection of predictor data.
SR267	AAU	AAU	FMU	A Risk Prediction Model for the Assessment and Triage of Women with Hypertensive Disorders of Pregnancy in Low-Resourced Settings: The miniPIERS (Pre-eclampsia Integrated Estimate of RiSk) Multi-country Prospective Cohort Study	Beth A. Payne	2014	Original research	1 July 2008 to 31 March 2012	5LMIC; Uganda , S/Africa, Brazil, India and Pakistan	Not specified	The objective of the miniPIERS study was to develop and validate a simplified clinical prediction model for adverse maternal outcomes among women with HDP for use in community and primary health care facilities in LMICs.	Prospective multicentre cohort	data were collected prospectively on 2,081 women with any hypertensive disorder of pregnancy admitted to a participating centre.	Women were excluded from the study if they were admitted in spontaneous labour, experienced any component of the adverse maternal outcome before eligibility or collection of predictor variables, or had confirmed positive HIV/AIDS status with CD4 count ,250 cells/ml or AIDS-defining illness.

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SR40	AAU	AAU	FMU	Intervention is MEWT plus recommended clinical evaluation and treatment guidelines related to the 4 focus areas while control sites had only the latter. Data was prospectively collected for 13 months (oct 2014 to october 2015). Baseline comparative data were derived from the 24-month time period (January 2012 through December 2013). To determine that the findings noted were not simply changes that would have been noted without the utilization of the MEWT tool, we also compared a control population from nonpilot sites during the same 2-year baseline and the 13 months of the MEWT trial.	NA	MEWT		Temperature, PR, RR, SBP, DBP, SPO2, FHR, Altered mental status anytime	Hospital-specific maternal early warning system locally developed based on clinical consensus with 7 parameters; Temperature (trigger >=38C, <=36c), SPO2 (trigger <=93%), HR (>110 or <50), RR (trigger >=24 or <12), Sys BP (trigger >155 or <80), diastolic BP (trigger >105 or <45), altered mental status anytime, FHR (trigger >160)	MEWT was developed based on data from review of the ICU admissions and basic elements of other reported early warning tools. The tool was designed to address 4 main etiologies of maternal morbidity: sepsis, cardiovascular dysfunction, severe preeclampsia-hypertension, and severe hemorrhage.	MEWT
SR22	AAU	AAU	FMU	The obstetric EWS was calculated based on secondary data collected during the first 24 hours of ICU dmission. The performance of the Obstetric Early Warning Score was evaluated using the area under the receiver operator characteristic curve. Outcomes selected were: maternal death, need for mechanical ventilation, and/or vasoactive support. Statistical methods included distribution appropriate univariate analyses and multivariate logistic regression.	NA	ICNARC clinical obstetric EWS		Temperature, PR, RR, SBP, DBP, FIO2 (96%), Level of consciousness	A statistically-based EWS (statistical OEWS), and a modification established by Carle et al based on the weight of each variable (clinical OEWS). The clinical OEWS score is calculated based on values of the following variables; sys BP, diastolic BP, RR, HR, FiO2 required to maintain an oxygen sarturation of >=96%, temperature and level of consciousnessSpecific scores were defined as follows: 0 for routine care, 1-3 in the aggregate score for low-grade response, 4-5 in the aggregate score or 3 in 1 abnormal vital sign for a medium response, and >=6 in the aggregate score for a high response	NA	ICNARC clinical obstetric EWS
SR69	AAU	AAU	FMU	The relevant MEOWS physiological parameters were recorded on the chart at admission and subsequently monitored according to the following frequency; women in labour, 4 hourly till 24 h after delivery and then once a day till discharge, PPH; 1 hourly for 4 h, then 4 hourly for next 24h and thereafter once a day till discharge, CS or other procedure under anaesthesia; 1 hourly for 6 h, then 4 hourly for next 48 h and then once a day till discharge, Blood transfusion; Immediately prior to start of transfusion and then 15 min into transfusion. Based on outcome at time of discharge, Category 1 (normal and recovered without morbidity) and Category 2 (recovered with morbidity or mortality) were defined. Performance of MEOWS chart as a screening tool was evaluated by calculating its sensitivity, specificity and predictive values using Exact's method. Relative risk of morbidity (odd's ratio) and 95% confidence interval was calculated for individual parameter.	NA	CEMACH MEOWS		Temperature, PR, RR, SBP, DBP, SPO2, FHR, AVPU, dipstick, liquor and lochia	Measurement of temperature (oral), heart rate, blood pressure, respiratory rate, oxygen saturation (pulse oximeter), conscious level (AVPU: alert, responds to voice or pain and unresponsive), proteinuria (urine dipstick test), colour of liquor and lochia characteristics are the parameters in the colour coded CEMACH MEOWS. A trigger was defined as a single markedly abnormal observation (red trigger) or the combination of two simultaneously mildly abnormal observations (two yellow triggers). However, no intervention was done based on trigger and patients were managed according to hospital protocol	NA	CEMACH MEOWS
SR5	AAU	AAU	FMU	All cases of maternal bacteraemia during the study period were identified from the laboratory database. After identification of the cases, One researcher (P.J.M.) reviewed all case notes and, in particular, the notes for the admission during which bacteraemia occurred. The IMEWS chart was applied retrospectively to cases before April 1, 2013 and applied prospectively to cases in the following 12 months	NA	IMEWS,		Temperature, PR, RR, SBP, DBP, FHR	A colour coded chart with 5 parameters; PR, RR, Sys BP, dias BP and temp. The chart sets out an escalation policy whereby women with one vital signs value in the red range or two values in the yellow range require medical review. The escalation guideline also states that, even in the setting of normal vital signs, medical review should be requested if staff have any concerns about a woman's condition.	NA	IMEWS,

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SR10	AAU	AAU	FMU	Physiological variables collected during the first 24 h of critical care admission were analysed. Logistic regression analysis for mortality in the model development set was initially used to create a statistically based early warning score. The statistical score was then modified to create a clinically acceptable early warning score. Important features of this clinical obstetric early warning score are that the variables are weighted according to their statistical importance. The statistical and clinical early warning scores were internally validated using the validation set.	NA	Statistical EWS and Clinical EWS		Temperature, PR, RR, SBP, DBP, FIO2 (96%), Level of consciousness (Clinical)	Statistical EWS; Consist of sys BP, RR, HR, FiO2 required to maintain SPO2>=96%, temperature, conscious level based on alert/not alert (15 or <15) and urine output. Clinical Obstetric EWS consist of the following parameters; sys BP, diastolic BP, RR, HR, %O2 required to maintain SPO2>=96%, temperature, conscious level all scored 0 to 3 (0 being normal) according to statistical significance.	fined as follows:0 for routine care, 1-3 in the aggregate score for low-grade response, 4-5 in the aggregate score or 3 in 1 abnormal vital sign for a medium response, and 6 in the aggregate score for a high response	Statistical EWS and Clinical EWS
SR61	AAU	AAU	FMU	Measurement of temperature (oral), blood pressure and heart rate, respiratory rate, oxygen saturation (pulse oximeter and arterial blood sampling where applicable), conscious level (AVPU: Alert, responds to Voice or Pain, and Unresponsive) and pain scores (0 = no pain, 1 = slight pain on movement, 2 = intermittent pain at rest/moderate pain on movement) were documented at least every 12 h.Outcome at 30 days was retrieved from the hospital record system and notes.The chi-squared test was used to compare the development of morbidity and the presence of emergency intervention in women who triggered, compared with those who did not	NA	CEMACH MEOWS		Temperature, PR, RR, SBP, DBP, SPO2, FHR, AVPU, dipstick, liquor and lochia	As previously described. A trigger was defined as a single markedly abnormal observation (red trigger), or the combination of two simultaneous mildly abnormal observations (two yellow triggers). A trigger prompted urgent medical assessment (Appendix 2)	NA	CEMACH MEOWS
SR33	AAU	AAU	FMU	A chart level review was performed for all ICU cases in the seven pilot hospitals. Demographic data, vital signs, symptoms, available pertinent notes, and intervention data were evaluated and collated, and then entered into a Microsoft Excel 2010 spreadsheet. The early intervention data included need for blood transfusion, treatment of severe hypertension, starting antibiotics within an hour of sepsis diagnosis, oxygen supplementation, and a call for provider bedside assessment. Matching data were assessed and collected for the control group in a separate database.The frequency and intervals of observation of MEWTs in the ICU group and control group were compared via Microsoft Excel, and odds ratios (ORs) and 95% confidence intervals (CIs) were generated using MedCalc (MedCalc Software, Ostend, Belgium).	NA	MEWTs		HR, MABP, RR, SPO2, Temp and Altered mental state	On the basis of the presenting symptoms and vital sign values in normal pregnancy described in several studies [5–7,11–13], the following MEWTs were assessed: heart rate (HR), including tachycardia (N110 beats per minute) or bradycardia (b50 beats per minute); mean arterial pressure (MAP) less than 65 mm Hg; respiratory rate (RR), including tachypnea (N24 breaths per minute) or bradypnea (b10 breaths per minute); low oxygen saturation (SpO2b 94%); abnormal temperature (AT; oral or aural), including high (≥38 °C) or low (b36 °C); and altered mental state (AMS), defined as confusion, agitation, persistent intensifying pain, and/or non-responsiveness	Low or high blood pressure was not included because, first, there are wide variations in low blood pressure that can be considered abnormal in pregnancy [11] and are best addressed by the MAP value; and second, high blood pressure is a component of an established standardized system diagnostic and treatment bundle for hypertension	MEWTs

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SR62	AAU	AAU	FMU	De-identified MEOWS variables plus six demographic variables (age, BMI, smoking status, gravidity, gestational age on admission, and birth weight) were extracted from the hospital case notes for the 24-hour period prior to ICU admission (cases) and the first 24 hours following admission (control patients). for multiple measurements, the most abnormal values were selected. for multiple measurements, the most abnormal values were selected.). Model performance was assessed based on sensitivity, specificity, and predictive values.	Following stepwise logistic regression, of eight significant variables identified using univariable analyses (P < 0.05; maximum temperature, maximum heart rate, minimum heart rate, maximum systolic blood pressure, minimum sBP, maximum diastolic blood pressure, minimum diastolic blood pressure, and respiratory rate), four variables were significantly associated with ICU admission >24 hours: maximum temperature (b co-efficient 1.14; P ¼ 0.005); heart rate (b 0.06; P < 0.001); sBP (b 0.05; P < 0.001); and respiratory rate (b 0.22; P ¼ 0.001).	CEMACH MEOWS		Temperature, PR, RR, SBP, DBP, SPO2, FHR, AVPU, dipstick, liquor and lochia	“MEOWS activation” was defined as the occurrence of 1 “red” or 2 “amber” MEOWS triggers.	NA	CEMACH MEOWS
SR44	AAU	AAU	FMU	NEWS was incorporated into the medical files of eligible obstetric patients. The nursing staff was responsible for monitoring patients undergoing emergency CS between 1700 hours and 0800 hours using NEWS. Prospective and retrospective review of medical records of all patients who had emergency C-section before (September-December 2013) and after (April-August 2014) the implementation of NEWS was conducted. We did not exclude any emergency CS done during the study duration. Maternal and perinatal outcomes of these patients were compared to assess the difference, ifany ,in patient's outcome. Rate of maternal and neonatal outcomes 6months before and after the implementation of NEWS was compared using Student's t-test, chi-square test and Fisher's exact test.	NA	NEWS	Score	BP, PR, RR, SPO2, Level of consciousness, Blood sugar	Through NEWS, a patient's vital signs (blood pressure, pulse, respiratory rate, oxygen saturation, level of consciousness and blood sugar) were recorded and each vital sign was allocated a numerical score (from 0 to 3) on a colour-coded observation chart, where a score of 0 was most desirable and a score of 3 was least desirable.	These scores were then aggregated and the total score was recorded which was their early warning score and could range from 0 to > 7. The lower the aggregate, the lower the risk for a patient and vice versa. Based on the aggregated score, escalation plan for monitoring and management of patient was also provided.Forexample,if a patient's score was 0 then 12-hourly monitoring was required, whereas if score was>7 continuous monitoring, immediately informing specialist/consultant concerned and transfer toi ntensive care unit(ICU) were advised	NEWS
SR35	AAU	AAU	FMU	Global literature databases (MEDLINE, PubMed) and clinical guidance publications were searched to identify working examples of early warning systems specifically used in maternity care. A care-quality database of patients transferred to intensive care was searched and electronic records reviewed by 1 member of the research team to identify cases for inclusion. Each set of vital signs (heart rate, respiratory rate, blood pressure, temperature, mental state) recorded during labour was retrieved from the electronic. For each woman the single worst composite set of recorded vital signs (generating the highest MEWS score) during the admission episode was selected. These vital signs were then used to generate early warning scores according to the instructions for each of the six MOEW systems. The proportion of cases reaching the warning trigger score was calculated for each system with 95% confidence intervals (CIs). Test characteristics (sensitivity, specificity, positive predictive value, negative predictive value) were calculated for each MOEWS trigger for severe sepsis, ICU transfer, or death . As a summary measure of the diagnostic performance of each test the receiver operating characteristic (ROC) curve was calculated along with the area under the ROC (AUROC).	NA	Six published MOEWS (A-F)		HR, BP, RR, Temp, Mental state,	Six published MOEWS (A-F) were identified representing the 2 most common methods of track-and-trigger early warning systems: color-coded trigger bands (single/multiple indicator trigger systems) and numerical scoring triggers (or aggregate-weighted scoring systems).14,15 The scoring thresholds for each system investigated in this study are outlined in Table 1. For each early warning system, the threshold score indicating the highest risk level that should prompt immediate senior medical review was identified as the trigger and was then used for further analysis	MOEWS were included if they had clear instructions, in English, such that the scoring system could be easily applied to a dataset of clinical vital sign observations. Chorioamnionitis was selected as the study group of interest as it represents a common diagnosis during the intrapartum period, which is the focus of this article.	Six published MOEWS (A-F)
SR40	AAU	AAU	FMU	The records of all women admitted to the HDU (n=167) between April 1, 2013 and March 31, 2014 were identified.. The IMEWS was considered to have had a role in the decision to admit patients if abnormal vital signs were recorded on IMEWS charts in the 2 hours preceding HDU transfer	NA	IMEWS,	colour	Temperature, PR, RR, SBP, DBP, FHR	The IMEWS is a paper chart completed with clinical case notes. Vital signs recorded on charts are color coded according to their value, using predefined thresholds for abnormalities. The IMEWS is used from the time of pregnancy diagnosis until 6 weeks postnatally, but other monitoring charts are used in operating theaters and labor wards. A standardized IMEWS escalation policy directs that medical review should be requested for patients with abnormal vital signs and for individuals with normal vital signs about whom there are clinical concerns	NA	IMEWS,

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SR26	AAU	AAU	FMU	Each set of vital signs (temperature, heart rate, blood pressure, and respiratory rate) that was recorded during labor was abstracted, with the exception of those taken within 40 minutes of epidural placement, given the transient changes in blood pressure and heart rate that may be associated with this procedure. Intrapartum characteristics (duration of labor and duration of rupture of membranes) and laboratory results were abstracted as well. After all data were collected, SIRS and MEWS scores were generated for each patient in the study cohort.The single MEWS score that was highest was selected for further analysis. We calculated the percentage of women who met SIRS criteria or who had a MEWS score of 5, with 95% CIs. Test characteristics (sensitivity, specificity, positive predictive value, negative predictive value) of both the SIRS andMEWS scoring systems in the prediction of the primary outcome (ICU transfer, sepsis, or death) were determined.	NA	MEWS	Score	Sbp,HR,RR,Temp and Mental state	MEWS has five parameters; sBP, HR, RR, Temperature and Mental status scored between 0 (normal) and 3 (severe derrangement, table 2). SIRS scores were either positive (>=2 criteria met) or negative. MEWS scores were considered “positive” at >=5, as defined in a previous study (ref no 4).	NA	MEWS
SR55	FMU	FMU	AAU	Adaptation and implementation of the MOEWS chart to the study hospital, piloting phase, retrospective study, introduction of the chart and spot checks audit was performed. A quality indicator was developed and applied in monitoring the use of MEOWS	Implemented as part of a quality improvement project	MOEWS, locally adopted by hospital maternity staff	colour		color coded early warning system chart, a details of parameters was not explicitly mentioned	N/A	MOEWS, locally adopted by hospital maternity staff
SR70	FMU	FMU	AAU	Inclusion and exclusion criteriawere set against which the cases were evaluated Clinical data were extracted and plotted on EWS charts. and descriptive analyses performed.	Not stated	EWS	Score	Level of consciousness Respiration rate Heart rate Systolic blood pressure Temperature	Level of consciousness Respiration rate Heart rate Systolic blood pressure Temperature	No patient had a complete set of respiratory rate, heart rate , blood pressure and temperature recordings	EWS
SR266	AAU	AAU	FMU	We developed and internally validated the fullPIERS model in a prospective, multicentre study in women who were admitted to tertiary obstetric centres with pre-eclampsia or who developed pre-eclampsia after admission. Routinely reported and informative variables were included in a stepwise backward elimination regression model to predict the adverse maternal outcome. To avoid collinearity, the correlation between variables was assessed and the more clinically relevant variable of a pair of highly correlated variables was included. We assessed performance using the area under the curve (AUC) of the receiver operating characteristic (ROC). Standard bootstrapping techniques were used to assess potential overfitting.	Customised case report forms and database were used by all participating sites. Data were obtained from patient medical records, and predictor variables were collected within 48 h of eligibility. If absent, the method of last observation carried forward was used by which any preceding observation recorded within 2 weeks of admission was regarded as current unless replaced by a more recent value. Although not universally supported, this method is consistent with clinical practice since clinicians do not re-evaluate what they believe has not changed, and is conservative in underderestimating the effect of any given variable in modelling.	fullPIERS			The model included gestational age at eligibility, chest pain or dyspnoea, SpO2, platelet count, serum Creatinine, and aspartate transaminase as predictors.		fullPIERS
SR267	AAU	AAU	FMU	Candidate predictors collected within 24 hours of admission were entered into a step-wise backward elimination logistic regression model to predict a composite adverse maternal outcome within 48 hours of admission. Model internal validation was accomplished by bootstrapping and external validation was completed using data from 1,300 women in the Pre-eclampsia Integrated Estimate of RiSk (fullPIERS) dataset. Predictive performance was assessed for calibration, discrimination, and stratification capacity. A final assessment of model validity was performed by applying the miniPIERS model to the fullPIERS dataset and estimating the AUC ROC	NA	miniPIERS			The final miniPIERS model included: parity (nulliparous versus multiparous); gestational age on admission; headache/visual disturbances; chest pain/dyspnoea; vaginal bleeding with abdominal pain; systolic blood pressure; and dipstick proteinuria.	NA	miniPIERS

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Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**13.Outcome measures and defining criteria (if applicable eg deaths, near-miss, ICU admission) or NA**	**14.Predictive properties of MEOWS parameters on outcomes in 13 or NA**	**14a. Performance of MEOWS as a screening tool (if applicable)e.g sensitivity, specificity, PPV, NPV, AUROC) or NA**	**14b. Performance of other monitoring charts (compared, if applicable eg predictive properties) or NA**	**14c. Performance of MEOWS compared to 14b**	**15. Findings (overall effect estimate on outcome measures, if applicable e.g prevalence of outcomes before and after MEOWS for studies testing effectiveness) or NA**
SR40	AAU	AAU	FMU	Primary outcome data were Centers for Disease Control and Prevention (CDC)-defined severe maternal morbidity and composite maternal morbidity. Composite maternal morbidity included CDC criteria with the addition of hemorrhage (>500 mL after vaginal delivery and 1000mL after cesarean delivery without trans-fusion), dilation and curettage, or ICU admission. Other outcome data included the screening rate for each hospital, the screen positive or alert rate for each pathway that was triggered, whether the clinical pathway was followed, and timeliness of provider responses. The rates of maternal sepsis, eclampsia, maternal hemorrhage without transfusion, hemorrhage with trans-fusion, hysterectomy, and dilation and curettage were also collected.	Analysis of performance of individual EWS parameters not perormed.	Sensitivity for ICU admission was 96.9%, specificity was 99.9% PPV of 12% and NPV was 99.9%.	NA	NA	During the 13 month period, there was a 5.5% nonsignificant increase in the rate of ICU admission at MEWT pilot sites (p=0.8) and an 8% nonsignificant decrease at nonpilot sites (p=0.4). There was a significant reduction in both CDC-defined severe maternal morbidity (-18.4%, p=0.01) and composite maternal morbidity (-13.6%, p=0.01) when comparing baseline and after implementation of the MEWT tool when the same baseline time period and 13- month MEWT trial time were compared at nonpilot sites, there was no change in CDC-defined severe maternal morbidity (p=0.6) and no change in the rate of composite morbidity (p= 0.9). When the 6 MEWT pilot sites were compared to 23 nonpilots sites there was a significantly lower rate of CDC-defined severematernal morbidity (p<.01) and composite maternal morbidity (p<.01)
SR22	AAU	AAU	FMU	Outcome measures were maternal death, need for mechanical ventilation, and/or vasoactive support	Crude and adjusted mortality risk analyses showed that abnormal systolic blood pressure, heart rate, temperature, FiO2 , and an abnormal GCS score were all significantly associated with mortality but abnormal values of diastolic blood pressure or respiratory rate were not (Table 2). Importantly, the variable with the highest ssociation with maternal death was a GCS score <=14 (abnormal level of consciousness), with an OR of 12.35 (95% CI, 5.26-29.02). The AUC of the ability of OEWS to discriminate mortality was 0.84 (95% CI, 0.75-0.92).	The OEWS value was significantly higher in nonsurvivors compared to survivors [12 (IQR 10-13) vs 7 (IQR 4-9); p <.001]. Mortality rate was significantly associated with a higher number of vital sign abnormalities (Jonckheere-Terpstra test; p < 0.001). Accordingly, for each increasing value of OEWS, mortality risk increased approximately 1.5 times (OR, 1.48; 95% CI, 1.30-1.69).	We have previously compared the performance of scoring systems for critically ill patients for the prediction of maternal death in the ICU, and along with others have shown that scores such as the Simplified Acute Physiology Score II and III, as well as the Acute Physiology And Chronic Health Evaluation (APACHE) II and the mortality probability model (MPM) III, overestimate maternal death	NA	Overall the predictive value was better in critical care admissions where the main cause of admission was directly related to pregnancy or the postpartum state. The AUC of the score in conditions directly related to pregnancy and postpartum was 0.87 (95% CI, 0.79-0.95), while in indirectly related conditions the AUC was 0.77 (95% CI, 0.58-0.96).
SR69	AAU	AAU	FMU	Obstetric morbidity or mortality. morbidity was defined based on a set of criteria on table 2	After adjusting for confounding factors i.e. age and underlying obstetric or medical condition at time of admission, the individual parameter trigger (i.e. abnormality in heart rate, systolic and diastolic blood pressure, temperature, neuroresponse) remained statistically significant (p < 0.001) for predicting risk of obstetric morbidity	Out of 284 patients who triggered on MEOWS charts, only 153 could meet the criteria of obstetric morbidity. There were 24 patients who had morbidity but did not trigger on MEOWS chart (Fig. 6). The MEOWS chart was found to be 86.4% sensitive, 85.2% specific and had a positive and negative predictive value of 53.87% and 96.9% respectively for predicting obstetric morbidity	NA	NA	MEOWS chart emerged as a useful bedside screening tool for prediction of obstetric morbidity and should be used routinely in every obstetric unit
SR5	AAU	AAU	FMU	Recording of vital signs, interval from IMEWS trigger	NA	NA	NA	NA	In the present study of women with maternal bacteraemia, the introduction of a national standardized obstetric EWS was associated with an improvement in the recording of vital signs, particularly respiratory rate. As compared with the 61 cases prior to IMEWS introduction, there was a reduction in the interval from IMEWS trigger to antibiotic administration, although this did not reach statistical significance (113 minutes versus 98 minutes; P = 0.384)

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Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**13.Outcome measures and defining criteria (if applicable eg deaths, near-miss, ICU admission) or NA**	**14.Predictive properties of MEOWS parameters on outcomes in 13 or NA**	**14a. Performance of MEOWS as a screening tool (if applicable)e.g sensitivity, specificity, PPV, NPV, AUROC) or NA**	**14b. Performance of other monitoring charts (compared, if applicable eg predictive properties) or NA**	**14c. Performance of MEOWS compared to 14b**	**15. Findings (overall effect estimate on outcome measures, if applicable e.g prevalence of outcomes before and after MEOWS for studies testing effectiveness) or NA**
SR10	AAU	AAU	FMU	Death	NA	ROC curves for the statistical EWS and clinical EWS are 0.995 (95% CI 0.992–0.998) and 0.957 (95% CI 0.923–0.991), respectively	The area under the ROC curves for the Swanton's empirically designed MEOWS was 0.955 (95% CI 0.922–0.988) [5]; the obstetric EWS provided in the 2003–2005 CEMACH Report was 0.937 (95% CI 0.884– 0.991) and the Royal College of Physicians NEWS 0.973 (95% CI 0.957–0.989)	The AUROC for these three scores, whilst outperformed by the statistical EWS (0.995 (95% CI 0.992–0.998)), are broadly similar to that of our clinical EWS (0.957 (95% CI 0.923–0.991)). Although this is a superficial comparison, it suggests some degree of construct validity to MEOWS, the CEMACH obstetric EWS and NEWS. We can therefore comment that our obstetric EWS, which has been developed using critical care data, performs in a similar manner in this analysis to the obstetric and non-obstetric EWS that are based on ward data. This similarity in performance suggests that our clinical EWS may also perform well when applied to ward-based data.	the new clinical obstetric early warning score has an excellent ability to discriminate survivors from non-survivors in this critical care data set.
SR61	AAU	AAU	FMU	morbidity, death, intensive care unit (ICU) admission, discharged alive.The definitions of maternal morbidity were agreed jointly by the authors at the beginning of the study (Table 2)	Overall, women who triggered were more likely either to have or to develop morbidity than those who did not (39% vs < 1%, respectively, p < 0.0001). They were also more likely to have undergone an emergency obstetric intervention (caesarean section, ventouse or forceps delivery): 46% vs 16%, respectively, p < 0.0001. The median (IQR [range]) hospital stay in women who triggered was 3 (1–4 [1–27]) days vs 1 (1-2 [1–21]) days in the women who did not trigger (p < 0.0001).	The overall sensitivity of MEOWS in predicting morbidity was 89% (95% CI 81–95%), specificity 79% (95% CI 76–82%), positive predictive value 39% (95% CI 32–46%) and negative predictive value 98% (95% CI 96–99%).	NA	NA	This study suggests that MEOWS is a useful bedside tool for predicting morbidity
SR33	AAU	AAU	FMU	ICU Admission	The ICU group had a significantly higher frequency of tachycardia as compared with the control group. The mean HR was 130.83 ± 16.34 beats per minute in the ICU group and 107.65 ± 22.28 beats per minute in the control group. The ICU patients also had a higher frequency of MAP less than 65 mm Hg (Pb 0.001). Compared with the control patients, the ICU patients more frequently had a temperature greater than 38 °C (Pb 0.010) and AMS. Although the frequency of RR greater than 24 breaths per minute was higher in the ICU group, the difference was not significant. The frequency of SpO2 less than 94% did not differ significantly between the groups (P = 0.076). The presence of two or more MEWTs was seen more frequently in ICU patients than in normal obstetric patients (Pb 0.001) (Table 3). Of the 10 patients in the control group with at least two MEWTs, the MEWTs did not persist in either the active phase or the second stage of labor. By contrast, all 36 ICU patients with at least two MEWTs had MEWTs that persisted for 30 minutes or more. On the basis of this analysis, MEWTs were defined as persistent if they lasted for 30 minutes or more. Via this definition, only two control patients had persistent MEWTs while in labor, as opposed to 36 patients needing ICU admission (Table 3). The presence of two or more MEWTs would give a detection rate of 72% but a false-positive rate of 20%. With the definition of persistent MEWTs (two or more triggers lasting more than 30 minutes), the false-positive screen rate would be decreased to 4% without altering the	Using trigger threshold at ≥2 MEWTs, sensitivity, specificity, PPV and NPV were 72 (57–83), 80 (66–90), 78 (63–89) and 74 (60–85) respectively. whereas ≥2 persistent MEWTs produced sensitivity, specificity, PPV and NPV of 72 (57–83), 96 (85–99), 95 (81–99), and 77 (65–87) respectively	NA	NA	Persistent MEWTs were present in most obstetric ICU cases. Retrospectively, MEWTs in this cohort seemed to separate normal obstetric patients from those for whom ICU admission was indicated; their use might reduce maternal morbidity. Also, the present findings indicated that two or more MEWTs persisting over 30 minutes or more might be better at identifying obstetric patients who require escalation of care

ARTICLE									
Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**13.Outcome measures and defining criteria (if applicable eg deaths, near-miss, ICU admission) or NA**	**14.Predictive properties of MEOWS parameters on outcomes in 13 or NA**	**14a. Performance of MEOWS as a screening tool (if applicable)e.g sensitivity, specificity, PPV, NPV, AUROC) or NA**	**14b. Performance of other monitoring charts (compared, if applicable eg predictive properties) or NA**	**14c. Performance of MEOWS compared to 14b**	**15. Findings (overall effect estimate on outcome measures, if applicable e.g prevalence of outcomes before and after MEOWS for studies testing effectiveness) or NA**
SR62	AAU	AAU	FMU	The primary outcome was maternal ICU admission >24 hours.	NA	The model using the MEOWS components (either 1 red or 2 amber scores) had high sensitivity (0.96) but low specificity (0.54) for identifying women at risk of ICU admission >24 hours. (PPV=0.41 and NPV=0.97);1 red trigger maintained sensitivity (0.96) and improved specificity (0.73); 2 red triggers lowered sensitivity (0.65) and increased specificity (0.89).	The AUROC for thefour-variable equation was 0.91 (95% CI 0.83 to 0.95), with activation of 1 red or 2 amber triggers providing high sensitivity, specificity, and NPV (0.87, 0.84 and 0.95 respectively) and slightly improved PPV (0.65)	No comparison could be made with a development data set because CEMACH MEOWS was developed by arbitrarily assigning cut-offs.	Altering MEOWS trigger parameters may improve the accuracy ofMEOWS in predicting ICU admission. Formal modelling of a MEOWS scoring system is required to support evidence-based care
SR44	AAU	AAU	FMU	Several maternal and neonatal health outcomes were observed as indicators of improved clinical care of patients. The maternal outcomes are; number of patients transfer to high level of care 6 month before and after implementation, number of patients needed consultancy with specialist, maternal complications (postpartum haemorrhage, need for blood transfussion, anaesthesia complications) and number of maternal deaths.	NA	NA	NA	NA	After implementation of NEWS, none of the patients needed consultancy with specialist or admission to ICU or tertiary care and were managed well at the secondary level. Moreover, 3(3%) patients were referred before implementation due to postoperative complications whereas none was referred after implementation. No maternal deaths were recorded. No significant difference was found in time interval for decision made for emergency CS and action taken (p=0.16). Of all, 13 (6.5%) patients had post-Partum haemorrhage after CS; they all belonged to Group A (p=0.00). Blood was transfused to only 2(1%) patients, both from Group A (p=0.15).
SR35	AAU	AAU	FMU	severe sepsis, ICU transfer, or death .	**Our data showed that the range of sensitivities of the 4 tested MOEWS went as low as 40%, compared with 100% for the MEWS. And the lowest specificity was just 3.9%, compared to 90.4% for MEWS. Moreover, the MEWS achieved both high sensitivity (100%) and specificity (90.4%) whereas the highest specificity of 96% in the MOEWS that we tested was associated with a sensitivity of only 40%. The best performing MOEWS (MOEWS D) had an AUROC of 0.72, which suggests the test has only moderate discriminatory power, and the AUROC for MOEWS B and C suggests that these systems are little better than chance at predicting poor outcome in sepsis. Even though it had the best AUROC profile, MOEWS D failed to identify 2 (40%) of the 5 women who developed severe sepsis. It is unclear why MEWS should perform better than the scoring systems modified for use in maternity. It is possible, however, that modifications of thresholds in MOEWS used to enhance diagnostic power for other general obstetric conditions such as hypertension might have reduced the predictive power of the systems in this cohort of women with chorioamnionitis**	There was considerable variation in diagnostic power between each of the MOEWS tested; sensitivities ranged from 40% for MOEWS E to 100% for MOEWS A to C, with low positive predictive values for each of the MOEWS, which ranged from 1.42% (MOEWS C) to 15.4% (MOEWS E). The AUROC ranged from 0.52 (MOEWS B and C) to 0.72 (MOEWS D)	Standard MEWS for non-obstetric population; Sensitivity 100 (47.8 -100), specificity 90.4 (87.7 - 91.8), PPV 5.15 (1.69-11.6), NPV of 00 (99.5-100) and AUROC of 0.95 (0.94-0.96)	Refer to 14: None of the six MOEWS performed as well as the standard MEWS in predicting deterioration in these pregnant women with suspected infection	Currently used MOEWS vary widely in terms of alert thresholds, format, and accuracy. Most MOEWS have not been validated. The MOEWS generally performed poorly in predicting severe sepsis in obstetric patients; in general severe sepsis was overdetected. Simple MOEWS with high sensitivity followed with more specific secondary testing is likely to be the best way forward. Further research is required to develop early warning systems for use in this setting.
SR40	AAU	AAU	FMU	ICU Admission	NA	Of the 80 patients identified, IMEWS use had triggered clinical review in 59 (73.8%) patient admissions, with the response triggering rate varying across clinical conditions. While clinical review leading to HDU admission was triggered by the IMEWS in a majority of the 80 individuals monitored using the IMEWS, escalation to HDU admission depended on clinical judgement alone for approximately a quarter of these patients	NA	NA	The present study confirms that the introduction of the IMEWS has contributed to the early identification of critically ill obstetric patients; however such a system cannot replace clinical judgement.

ARTICLE									
Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**13.Outcome measures and defining criteria (if applicable eg deaths, near-miss, ICU admission) or NA**	**14.Predictive properties of MEOWS parameters on outcomes in 13 or NA**	**14a. Performance of MEOWS as a screening tool (if applicable)e.g sensitivity, specificity, PPV, NPV, AUROC) or NA**	**14b. Performance of other monitoring charts (compared, if applicable eg predictive properties) or NA**	**14c. Performance of MEOWS compared to 14b**	**15. Findings (overall effect estimate on outcome measures, if applicable e.g prevalence of outcomes before and after MEOWS for studies testing effectiveness) or NA**
SR26	AAU	AAU	FMU	ICU transfer, sepsis, or death	NA	At a threshold of 5 (which has been used as a clinically relevant threshold), the sensitivity, specificity, and positive and negative predictive values were 100%, 90.4%, 0.05%, and 100%, respectively	SIRS test characteristics for analysis with complete data had sensitivity, specificity, PPV and NPV of 100, 17.6, 100 and 1.7% respectively, while with assumption that all missing values were normal, the test chaeracteristics included sensitivity, specificity, PPV and NPV of 100, 37.2, 100 AND 0.9 respectively	MEWS also performed poorly as a predictive model in our obstetric population	SIRS and MEWS criteria do not identify accurately patients who are at risk for intensive care unit transfer, sepsis, or death among pregnant women with intrauterine infection and should not be used in an obstetric setting
SR55	FMU	FMU	AAU	Proportion of women in whom preoperative stablisation was performed. Proportion of women in whom action was taken as a result of the chart system.	N/A	N/A	N/A	N/A	Significant improvement in preoperative stabilisation (odds ratio 2.78 95% confidence interval 1.39 - 5.54) Significant improvement in action taken fro,m 4% to 62% (P<0.001)
SR70	FMU	FMU	AAU	Reason for admission to ICU/HDU early warning scoring scores at admission	N/A	N/A	N/A	N/A	Multidisciplinary team review determined that ana EWS might have reduced the seriousness of maternal morbidity in five cases (7.6%) including 3 admissions for obstetric sepsis to ICU , two to obstetric HDU for post partum haemorrhage.
SR266	AAU	AAU	FMU	The components of the combined adverse maternal outcome were: maternal mortality or one or more serious CNS, cardiorespiratory, hepatic, renal, or haematological morbidity. This outcome was developed by iterative Delphi consensus.	fullPIERS successfully stratified the population into clinically relevant risk categories (table 4), with a large percentage (65%) of women classifi ed into a low-risk group (predicted probability of <0・025), and 4% of women into the highest risk group (predicted probability ≥0・30). The majority (59%) of women with a predicted probability of 0・30 or greater had an adverse outcome. Conversely, the adverse outcome only occurred in 1% of women with a predicted probability lower than 0・025, and in less than 1% of women with a predicted probability lower than 0・01 (negative predictive value >99%).	Developed with data from 1935 women with complete data (of the 2023 in the cohort in total), fullPIERS predicted adverse maternal outcomes within 48 h of eligibility (AUC ROC 0.88, 95% CI 0・84–0・92)	Preliminary assessments of fullPIERS in a broader range of women with pregnancy hypertension confirmed its performance (ie, AUC ROC >0・7). The AUC ROC for fullPIERS was 0・77 (95% CI 0・45–1・00) for women admitted to level 1 or 2 centres with preeclampsia (six outcomes in 139 women), 0・85 (95% CI 0・65–1・00) for those admitted to one tertiary centre (level 3) with a non-pre-eclampsia hypertensive disorder of pregnancy (four outcomes in 224 women), and 0・80 (95% CI 0・66–0・94) in those with pre-eclampsia admitted to centres in countries with low and middle incomes (17 outcomes in 145 women).	NA	fullPIERS accurately predicted adverse maternal outcomes for up to 48 h, a clinically useful period that allows steroid administration, transfer, or induction. Also, fullPIERS maintained good performance (AUC ROC >0・8) beyond 3 days post-eligibility and maintained reasonable performance The fullPIERS model identifi es women at increased risk of adverse outcomes up to 7 days before complications arise and can thereby modify direct patient care (eg, timing of delivery, place of care), improve the design of clinical trials, and inform biomedical investigations related to pre-eclampsia.(AUC ROC >0・7) up to 7 days post-eligibility.
SR267	AAU	AAU	FMU	The components of the composite adverse maternal outcome to be predicted by the model were determined by Delphi consensus [13] and include maternal mortality or one or more of serious central nervous system, cardiorespiratory, renal, hepatic,haematological, or other morbidity.	na	. The miniPIERS model was well-calibrated and had an area under the receiver operating characteristic curve (AUC ROC) of 0.768 (95% CI 0.735–0.801) with an average optimism of 0.037. External validation AUC ROC was 0.713 (95% CI 0.658–0.768). A predicted probability $25% to define a positive test classified women with 85.5% accuracy	When the miniPIERS model was applied to the fullPIERS dataset the AUC ROC was 0.713 (95% CI 0.658–0.768) after adjusting the model intercept to account for differences in the outcome rate between the fullPIERS and miniPIERS populations	na	The miniPIERS model shows reasonable ability to identify women at increased risk of adverse maternaloutcomes associated with the hypertensive disorders of pregnancy. It could be used in LMICs to identify women who would benefit most from interventions such as magnesium sulphate, antihypertensives, or transportation to a higher level of care.

ARTICLE I				QA (D1. Patient selection)			QA(D2. Indext test, EWS)			QA(D3. reference standard)			QA(D4. Flow of participants)	
Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**a. was a continuous or random sample of participants enrolled? (yes, no, unclear)**	**b. did the study avoid unnecessary exclussions?(yes, no, unclear)**	**C. are there concerns that the included participants do not match thereview question? (yes, no, unclear)**	**a. were the reference range adjusted for physiological change in pregnancy? (yes, no, unclear)**	**b. was the trigger threshold prespecified?(yes, no, unclear)**	**c. are there concerns that the index test, its conduct or interpretation differ from review question? (yes, no, unclear)**	**a. is the index test compared to a reference standard (or routine practice)? answer could be yes, no, unclear**	**b. were the reference standard results interpreted without knowledge of the results of the index test?(yes, no,**	**c. are there concerns that the target condition as defined by the reference standard does not match the review question?**	**a. is the attrition rate acceptable (<20%)?(yes, no, unclear)**	**b. could the dropped out participants (missing data) be systematically similar to those who completed? (yes, no,**
SR40	AAU	AAU	FMU	Yes	yes	no	yes	yes	no	yes	unclear	no	no	Unclear
SR22	AAU	AAU	FMU	yes	yes (only 3% excludeddue to incomplete vitals)	no	yes	yes	no	yes (diagnosed in routine care)	yes (retrospective analysis, outcome already defined)	no	yes (3%)	Unclear
SR69	AAU	AAU	FMU	Yes	yes	No	yes	yes	no	No	No	NA	yes	Yes
SR5	AAU	AAU	FMU	Yes	Unclear	Yes	yes	yes	no	NA	NA	NA	Yes (17.6%)	No

ARTICLE I				QA (D1. Patient selection)			QA(D2. Indext test, EWS)			QA(D3. reference standard)			QA(D4. Flow of participants)	
Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**a. was a continuous or random sample of participants enrolled? (yes, no, unclear)**	**b. did the study avoid unnecessary exclussions?(yes, no, unclear)**	**C. are there concerns that the included participants do not match thereview question? (yes, no, unclear)**	**a. were the reference range adjusted for physiological change in pregnancy? (yes, no, unclear)**	**b. was the trigger threshold prespecified?(yes, no, unclear)**	**c. are there concerns that the index test, its conduct or interpretation differ from review question? (yes, no, unclear)**	**a. is the index test compared to a reference standard (or routine practice)? answer could be yes, no, unclear**	**b. were the reference standard results interpreted without knowledge of the results of the index test?(yes, no,**	**c. are there concerns that the target condition as defined by the reference standard does not match the review question?**	**a. is the attrition rate acceptable (<20%)?(yes, no, unclear)**	**b. could the dropped out participants (missing data) be systematically similar to those who completed? (yes, no,**
SR10	AAU	AAU	FMU	Yes	Yes	No	Yes	No	No	yes (Swanton et al EWS, CEMACH MEOWS and NEWS)	unclear	No	No (Values of respiratory rate for non-ventilated non-survivors were missing in 85% and ventilated survivors in 55%. Lowest total GCS variable values were missing in 41% of non-survivors and 22% of survivors)	No
SR61	AAU	AAU	FMU	Yes	Yes	no	Yes	yes	no	No	Unclear	No	Yes (0.4%)	Yes
SR33	AAU	AAU	FMU	Yes	No (Excluded direct admission to ICU from theatre, emergency or refered patients)	no	yes	yes	no	no	no	NA	Yes	Yes

ARTICLE I				QA (D1. Patient selection)			QA(D2. Indext test, EWS)			QA(D3. reference standard)			QA(D4. Flow of participants)	
Article's ID Number	**Original Reviewer**	**Data abstracted by**	**Data abstraction checked by**	**a. was a continuous or random sample of participants enrolled? (yes, no, unclear)**	**b. did the study avoid unnecessary exclussions?(yes, no, unclear)**	**C. are there concerns that the included participants do not match thereview question? (yes, no, unclear)**	**a. were the reference range adjusted for physiological change in pregnancy? (yes, no, unclear)**	**b. was the trigger threshold prespecified?(yes, no, unclear)**	**c. are there concerns that the index test, its conduct or interpretation differ from review question? (yes, no, unclear)**	**a. is the index test compared to a reference standard (or routine practice)? answer could be yes, no, unclear**	**b. were the reference standard results interpreted without knowledge of the results of the index test?(yes, no,**	**c. are there concerns that the target condition as defined by the reference standard does not match the review question?**	**a. is the attrition rate acceptable (<20%)?(yes, no, unclear)**	**b. could the dropped out participants (missing data) be systematically similar to those who completed? (yes, no,**
SR62	AAU	AAU	FMU	Yes	yes	no	yes	yes	no	yes	no	no	no (non vital parameters poorly measured and precluded)	no
SR44	AAU	AAU	FMU	Yes	Yes	no	no (NEWS)	yes (Score high for risk of bias, justify further)	Yes	NA	NA	NA	Yes, (no exclusion made)	Yes
SR35	AAU	AAU	FMU	Yes	no (Excluded 39.8% of eligible participants due to incomplete vital signs record)	no	yes	yes	no	yes	Yes	no	no (39.8%)	no
SR40	AAU	AAU	FMU	Yes	No	no	yes	yes	no	no	NA	NA	No (>50%)	No

ARTICLE I				QA (D1. Patient selection)			QA(D2. Indext test, EWS)			QA(D3. reference standard)			QA(D4. Flow of participants)	
Article's ID Number	Original Reviewer	Data abstracted by	Data abstraction checked by	a. was a continuous or random sample of participants enrolled? (yes, no, unclear)	b. did the study avoid unnecessary exclussions?(yes, no, unclear)	C. are there concerns that the included participants do not match thereview question? (yes, no, unclear)	a. were the reference range adjusted for physiological change in pregnancy? (yes, no, unclear)	b. was the trigger threshold prespecified?(yes, no, unclear)	c. are there concerns that the index test, its conduct or interpretation differ from review question? (yes, no, unclear)	a. is the index test compared to a reference standard (or routine practice)? answer could be yes, no, unclear	b. were the reference standard results interpreted without knowledge of the results of the index test?(yes, no,	c. are there concerns that the target condition as defined by the reference standard does not match the review question?	a. is the attrition rate acceptable (<20%)?(yes, no, unclear)	b. could the dropped out participants (missing data) be systematically similar to those who completed? (yes, no,
SR26	AAU	AAU	FMU	Yes	no	no	no (MEWS)	yes	Yes	yes	yes	no	no	no
SR55	FMU	FMU	AAU	No	Yes	NO	Yes	Yes	No	unclear	Unclear	No	Yes	Yes
SR70	FMU	FMU	AAU	NO	NO	YES	Unclear	YES	Unclear	NO	NO	NO	Unclear	YES
SR266	AAU	AAU	FMU	Yes	yes	no	yes	no	yes (pre-eclampsia risk prediction-narrow with no broad coverage to obstetric complications)	NA	NA	NA	yes (88/2023 missing = 4.3%)	Yes
SR267	AAU	AAU	FMU	Yes	yes	no	yes	No	yes (pre-eclampsia risk prediction-narrow with no broad coverage to obstetric complications)	no	NA	NA	No	Yes

PLOS ONE

RESEARCH ARTICLE

Early warning systems in obstetrics: A systematic literature review

Aminu Umar[1], **Charles A. Ameh**[1]*, **Francis Muriithi**[2], **Matthews Mathai**[1]

1 Centre for Maternal and Newborn Health, Liverpool School of Tropical Medicine, Liverpool, United Kingdom, **2** Blackpool Teaching Hospitals National Health Service Foundation Trust, Blackpool, United Kingdom

* Charles.Ameh@lstmed.ac.uk

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Abstract

Introduction

Several versions of Early Warning Systems (EWS) are used in obstetrics to detect and treat early clinical deterioration to avert morbidity and mortality. EWS can potentially be useful to improve the quality of care and reduce the risk of maternal mortality in resource-limited settings. We conducted a systematic literature review of published obstetric early warning systems, define their predictive accuracy for morbidity and mortality, and their effectiveness in triggering corrective actions and improving health outcomes.

Methods

We systematically searched for primary research articles on obstetric EWS published in peer-reviewed journals between January 1997 and March 2018 in Medline, CINAHL, SCOPUS, Science Direct, and Science Citation Index. We also searched reference lists of relevant articles and websites of professional societies. We included studies that assessed the predictive accuracy of EWS to detect clinical deterioration, or/and their effectiveness in improving clinical outcomes in obstetric inpatients. We excluded studies with a paediatric or non-obstetric adult population. Cross-sectional and qualitative studies were also excluded. We performed a narrative synthesis since the outcomes reported were heterogeneous.

Results

A total of 381 papers were identified, 17 of which met the inclusion criteria. Eleven of the included studies evaluated the predictive accuracy of EWS for obstetric morbidity and mortality, 5 studies assessed the effectiveness of EWS in improving clinical outcomes, while one study addressed both. Sixteen published EWS versions were reviewed, 14 of which included five basic clinical observations (pulse rate, respiratory rate, temperature, blood pressure, and consciousness level). The obstetric EWS identified had very high median (inter-quartile range) sensitivity—89% (72% to 97%) and specificity—85% (67% to 98%) but low median (inter-quartile range) positive predictive values—41% (25% to 74%) for predicting morbidity or ICU admission. Obstetric EWS had a very high accuracy in predicting death (AUROC >0.80) among critically ill obstetric patients. Obstetric EWS improves the

frequency of routine vital sign observation, reduces the interval between the recording of specifically defined abnormal clinical observations and corrective clinical actions, and can potentially reduce the severity of obstetric morbidity.

Conclusion

Obstetric EWS are effective in predicting severe morbidity (in general obstetric population) and mortality (in critically ill obstetric patients). EWS can contribute to improved quality of care, prevent progressive obstetric morbidity and improve health outcomes. There is limited evidence of the effectiveness of EWS in reducing maternal death across all settings. Clinical parameters in most obstetric EWS versions are routinely collected in resource-limited settings, therefore implementing EWS may be feasible in such settings.

Abbreviations: AUROC, Area Under Receiver Operating Characteristic Curve; **CDC**, Centre for Disease Control; **CEMACH**, Confidential Enquiry into Maternal and Child Health; **EWS**, Early Warning Systems; **ICU**, Intensive Care Unit; **IMEWS**, Irish Maternity Early Warning System; **MEOWS**, Modified Early Obstetric Warning Systems; **MEWT**, Maternal Early Warning Triggers; **NEWS**, National Early Warning System; **NPV**, Negative Predictive Value; **PPV**, Positive Predictive Value; **RANZCOG**, Royal Australian and New Zealand College of Obstetricians and Gynaecologists; **SASOG**, South African Society of Obstetricians and Gynaecologists; **RCOG**, Royal College of Obstetricians and Gynaecologists; **WHO**, World Health Organization.

Introduction

The World Health Organization (WHO) estimated 303, 000 maternal deaths globally in 2015 at the end of the Millennium Development Goals era [1]. Over 99% of these deaths occurred in low-income settings [1]. It is also estimated that there were 27 million episodes of direct obstetric complications annually that contribute to long-term pregnancy and childbirth complications [2]. Good quality care including timely identification and management of obstetric complications can contribute to reducing the burden of maternal deaths and associated long-term complications [2].

Early Warning Systems comprise clinical observation charts and algorithms for triggering corrective action to improve clinical outcomes. Early warning systems have been used in non-obstetric specialties since 1997 [3]. EWS combine clinical observations such as vital signs, clinical examination findings and laboratory tests to identify a pattern that is consistent with an increased risk of clinical deterioration. A trigger is defined as a single markedly abnormal observation or a combination of mildly abnormal observations. When a trigger is observed, it is expected that actions by the care team using a predefined protocol/algorithm will significantly reduce the risk of an adverse outcome[4]. Physiological clinical observations such as vital signs are different in pregnant women compared to non-pregnant women as are abnormal thresholds [5]. Modified early warning systems for the obstetric population have been advocated because they enable early detection of clinical deterioration, presenting an opportunity for timely actions to improve clinical outcome (Fig 1) [6].

The Saving Mothers' Lives report of the United Kingdom's Confidential Enquiry into Maternal Deaths (CEMDs) 2005 strongly recommended the adoption of EWS modified for the obstetric population [6]. Since then, EWS has been widely adopted for use in hospital maternities internationally. A survey of 130 UK hospital anaesthetists in 2014 identified different versions of obstetric EWS (varying number of clinical observations and pathophysiological thresholds to trigger clinical action); however, none of these was considered as the gold standard [7].

A systematic review of the effectiveness of obstetric EWS by Betesh et al. (2013) reported no direct evidence of improved clinical outcomes based on the two included observational studies with uncertain outcome measures [4,8,9]. Since that review, several obstetric EWS studies have been conducted, assessing the predictive accuracy of obstetric EWS for adverse outcomes, and their effectiveness in improving clinical outcomes. To the best of our knowledge, there has

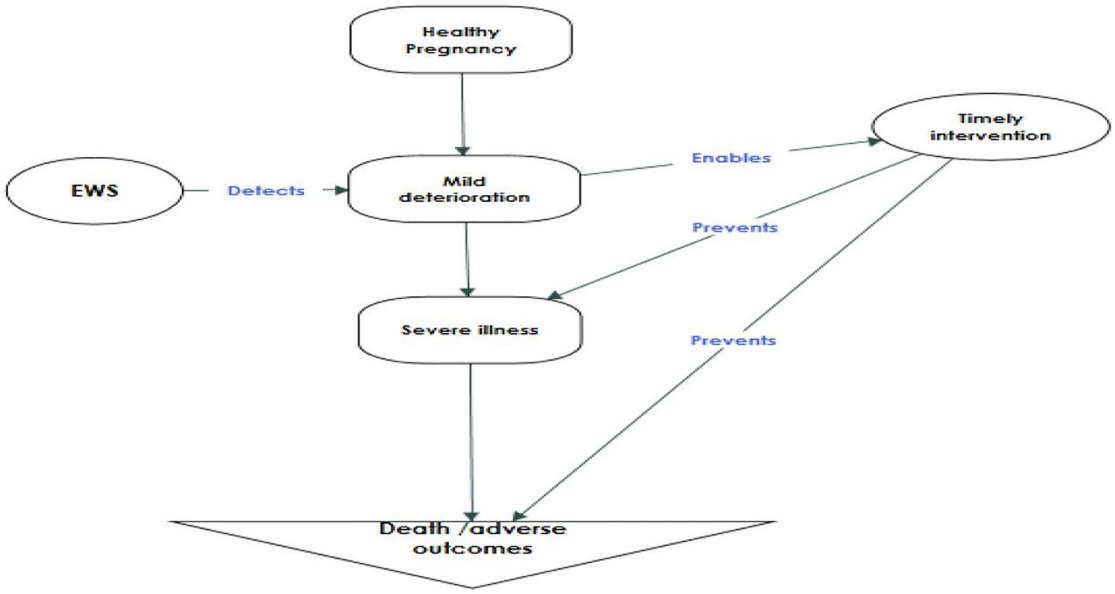

Fig 1. Hypothesis of the EWS intervention.

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not been an up-to-date synthesis of evidence on the overall usefulness of EWS in obstetric practice.

The objectives of this systematic review were (1) to synthesise the evidence on effectiveness of obstetric EWS as screening tools for morbidity and mortality (predictive accuracy) and (2) to determine the effectiveness of the EWS trigger systems in improving clinical outcomes, and to explore the feasibility of their implementation in low resource settings.

Methods

Study design

Systematic review methodology was adopted to achieve the study objectives based on the principles and methods provided by the York University's Centre for Reviews and Dissemination guideline. [10] The review findings were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [11].

Criteria for study selection

Study designs including prospective and retrospective longitudinal, case-control, cohort, quasi-experimental, step-wedge and randomized controlled trials were included if they possessed the following characteristics:

Participants. Pregnant women in labour, sick pregnant women of any gestational age and women who had recently given birth (within 6 weeks of delivery) admitted to hospital units including intensive care and high dependency units.

Intervention. Use of an obstetric EWS, including both paper-based and electronic monitoring systems.

Comparisons. Use of a non-obstetric EWS on an obstetric unit, usual care practice with no use of any EWS.

Outcome measures. Clinical outcomes: Maternal death, non-severe maternal morbidity, potentially life-threatening conditions, maternal near miss, intensive care unit admission.

Trigger system: the need for a specialist review, referral for a higher level of care, the interval between a trigger and corrective clinical action.

Search strategy

A preliminary search was conducted for existing reviews in the Cochrane central register, the three databases of the Centre for Reviews and Dissemination (Database of Abstract of Reviews of Effectiveness, Health Technology Assessment Database, and the NHS Economic Evaluation Database), Turning Research Into Practice (TRIP) Database and for ongoing reviews in PROSPERO.

We conducted a primary search of Medline, CINAHL, Scopus, Science Direct and Science Citation Index databases. We used search strategies that comprised a combination of text words and synonyms related to the intervention and outcomes of interest; search terms Appendix A in S1 Table. A systematic review expert at the Liverpool School of Tropical Medicine reviewed the search strategy that was subsequently piloted before application on the relevant databases. We also searched reference lists of identified articles and professional society websites including World Health Organization (WHO), Royal College of Obstetricians and Gynaecologists (RCOG), American College of Obstetricians and Gynaecologists (ACOG), Centre for Disease Control (CDC), Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) and South African Society of Obstetricians and Gynaecologists (SASOG) for relevant publications. All relevant studies published between January 1997 to March 2018 in any language were included.

Study selection

Two reviewers (AU and FM) independently screened all potentially relevant titles for the eligibility criteria. Publications were selected in two phases: first by reviewing titles and subsequently by a full-text review. Differences in judgment were resolved through consensus in consultation with CA and MM. All studies that met the inclusion criteria were included. Authors of conference abstracts were contacted by email for full texts: where these were not available, abstracts were excluded.

Studies were also excluded if they were: a) Conducted on a paediatric or non-obstetric adult population, b) Of qualitative methodological designs, c) Commentaries, editorials or letters.

Data extraction

Data related to study title, author, design, setting, population, description of intervention used, outcomes and summary of findings of included studies were abstracted into a Microsoft Excel data abstraction sheet that was cross-checked and ratified by two reviewers.

Data analysis

A structured narrative synthesis of included studies was conducted using the European Social Research Council guidance on the conduct of narrative synthesis in systematic reviews [12]. Included studies were tabulated by study objective and or study population to produce a clear descriptive summary. Relationships were explored within and between included studies; themes and sub-themes were identified and organized to fit the review's objectives. The evidence was synthesized to provide a meaningful narrative. To determine the effectiveness of EWS as a screening tool for adverse obstetric outcomes, sensitivity, specificity, negative and positive predictive values, and Area Under Receiver Operating Characteristic Curve (AUROC) was analysed.

Quality assessment

Based on one of the objectives of this systematic review—to synthesize evidence on the diagnostic accuracy of obstetric EWS- the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool was used for assessing the quality of included studies [13]. QUADAS-2 defines quality in diagnostic accuracy studies as the degree to which the estimate of diagnostic accuracy avoids the risk of bias, and the extent to which included studies are applicable to the review's research questions. The included studies were assessed for risk of bias across four domains: patient selection, index test, reference standard and flow of participants [13]. Studies were also assessed for concerns about applicability across the first three domains. In accordance with the QUADAS-2 guidelines, the suggested signalling questions and scoring guideline were tailored to fit our review; Quality assessment tool Appendix B1 in S1 Table. We drew conclusions on the overall quality of included studies based on the frequency of low/high level of bias and low/high/unclear concerns about applicability in the four domains. We concluded that a study was of good quality when it had low-risk bias or concern about applicability in all four domains. A study was of moderate quality if it had no more than one unclear domain and no high risk of bias or concern about applicability. A study was of poor quality if it has more than one unclear domain or any high risk of bias/concern about applicability in the four domains.

The systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO-CRD42017077504).

Results

Our search identified 381 papers (Medline = 152, Scopus = 24, CINAHL = 43, Science Citation Index = 88, Science Direct = 49, Clinical trials. gov = 11 and other sources = 14). Ten publications were available only as conference abstracts; authors of six of these abstracts confirmed unavailability of full texts. Seventeen papers met the inclusion criteria and were included in the review Fig 2, S2 Table. All studies that assessed the predictive accuracy of EWS for adverse obstetric outcomes were observational studies.

Characteristics of included studies

Included studies fell into two thematic categories: studies that investigated the predictive accuracy of EWS for adverse obstetric outcomes (validation studies) and those that investigated the effectiveness of EWS in improving measured outcomes (clinical outcomes and measures of the effectiveness of the EWS trigger mechanism). The study characteristics, including design, participants, intervention, outcome measures and key findings of these studies are presented in Table 1. All reviewed studies were published between 2010 and 2017.

The studies were distributed across six high-income countries, 3 upper-middle-income countries (Colombia, South Africa, and Brazil), one lower-middle income (India) and two low-income countries (Zimbabwe, Uganda). There were two multi-country studies: one of these [14] was conducted in five high-income countries (Canada, Australia, New Zealand, and the UK), and the other [15] recruited participants from five low and middle-income countries, including India, Pakistan, Zimbabwe, Colombia, South Africa, and Brazil.

Twelve observational studies [4,5,9,15–23] assessed effectiveness of EWS in predicting obstetric morbidity and mortality (predictive accuracy); of these, seven [4,9,16,19,20,22,23] investigated accuracy of the tools in predicting adverse outcomes among all obstetric inpatients, of these two were prospective studies and four were retrospective studies. Five were validation studies that looked at specific obstetric outcomes associated with chorioamnionitis [5,21] and pre-eclampsia [14,15,17].

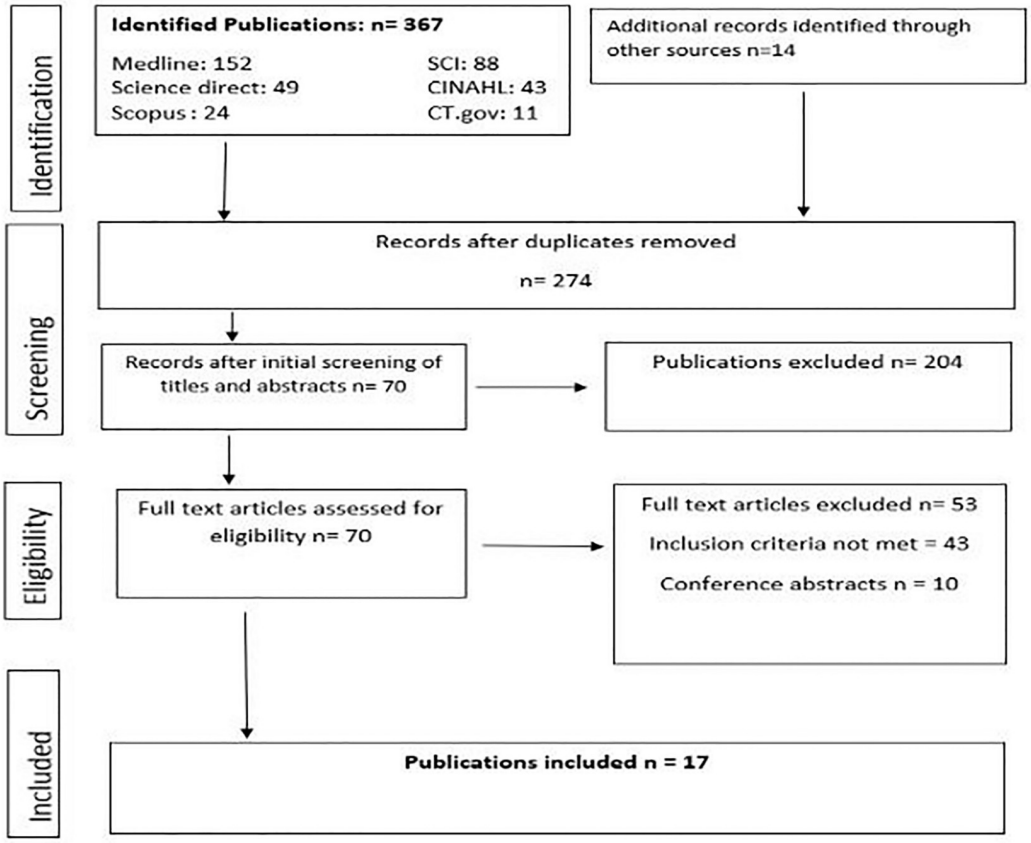

Fig 2. PRISMA diagram summarizing study selection process. Most of the studies that assessed the effectiveness of EWS in improving clinical outcomes were of quasi-experimental design.

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Four studies tested the effectiveness of EWS in reducing the prevalence of measured outcomes; the severity of morbidity [22,24], ICU admission [22,25,26] and pre-operative stabilisation [27]. Three studies reported on measures of EWS trigger effectiveness: referral rate for further care [26], change in frequency of vital sign monitoring [22], change in the interval between a trigger and corrective clinical action [27,28]. One study [22] assessed both the predictive accuracy of EWS and its effectiveness in improving clinical outcomes.

Quality of included studies

Based on the QUADAS-2 tool, a summary of the quality of all included studies is presented in Fig 3, while a detailed assessment of the quality of each included studies (risk of bias and concern about applicability) is provided as Appendix C in S1 Table.

Risk of bias. The majority of included studies had a low risk of bias for patient selection (65%), index test (82%) and the flow of participants (65%) Fig 3. The most common source of high risk of bias was the absence of a reference standard (4 studies), followed closely by the flow of participants or attrition bias in (3 studies), Fig 3. Just over a half of the included studies (9, 52%) had an unclear risk of bias for a reference standard; this was commonest among studies that assessed the effectiveness of EWS on measured outcomes Appendix C in S1 Table.

Concern about applicability. There was a high concern about the applicability of EWS used in four studies to this review's research questions: two studies used EWS that were not

Table 1. Summary of included studies.

Theme 1	Studies that tested the predictive accuracy of EWS on adverse obstetric outcomes				
Publication	**Design**	**Study Population**	**EWS type**	**Outcomes**	**Findings**
Lappen RJ et al., 2010	Retrospective cohort	Women with chorioamnionitis (n = 913)	MEWS and SIRS	Severe sepsis, ICU transfer, death	Both performed poorly (MEWS PPV = 5.4%, SIRS Specificity = 17.6%)
Von-Dadelszen P et al., 2011	Prospective Multicentre cohort study	Women admitted with pre-eclampsia or who developed pre-eclampsia in hospital (n = 1935)	fullPIERS model	Death, 1 or more serious CNS, cardiorespiratory, hepatic, renal, or haematological morbidity.	Predicted adverse maternal outcomes with AUROC of 0.88 (95% CI 0.84–0.92)
Singh S et al., 2012	Prospective observational study	Obstetric admissions from 20 weeks through to 6 weeks post-partum (n = 676)	CEMACH MEOWS	Outcome at 30 days-Morbidity based on consensus, death, ICU admission, discharged alive.	30% (200) triggered, 13% (86) had morbidity. Sensitivity 89% (95% CI 81–95%), Specificity 79% (95% CI 76–82%) PPV 39% (95% CI32-46%), NPV 98% (95% CI 96–99%)
Carle C et al., 2013	Retrospective analysis of secondary data	Obstetric admissions (n = 4440) to ICU	ICNARC obstetric EWS	Death	AUROC Statistical EWS = 0.99 Clinical EWS = 0.96
Payne et al., 2014	Prospective Multicentre cohort study	Women (n = 2081) with any hypertensive disorder of pregnancy admitted to a participating centre.	miniPIERS model	Death, 1 or more serious CNS, cardiorespiratory, hepatic, renal, or haematological morbidity	Predicted adverse maternal outcomes with AUROC of 0.77 (95% CI 0.74–0.80)
Edwards ES et al., 2015	Retrospective cohort	Women with chorioamnionitis (n = 913)	Six published MOEWS charts	Severe sepsis, death	AUROCs: A = 0.65 B = 0.52 C = 0.52 D = 0.72 E = 0.68 F = 0.65
Singh A et al., 2016	Prospective observational study	Women in labour beyond 28 weeks gestation, up to 6 weeks postpartum (n = 1065)	CEMACH MEOWS	Morbidity based on consensus	Sensitivity 86.4% Specificity 85.2% PPV 53.9% NPV 96.9%
Hedriana HL et al., 2016	Retrospective case-control study	Cases; Obstetric admissions to ICU (n = 50), Controls; SVD (n = 50)	MEWT	ICU admission	Sensitivity 72% (95% CI 57–83%) Specificity 96% (95% CI 85–99%) PPV 95% (95% CI 81–99%) NPV 77% (95% CI 65–87%)
Shields E L et al. 2016	Quasi-experimental	Obstetric admissions in 6 hospitals n = 11399	MEWT	ICU admission	Sensitivity 97% Specificity 99% PPV 12% NPV 99%
Ryan HM et al., 2017	Retrospective case-control study	Cases; 46 obstetric admissions to ICU, Controls; 138 admissions no critical care	CEMACH MEOWS	ICU admission for longer than 24 hours	Sensitivity 96% Specificity 54% PPV 41% NPV 97%
Paternina-Caicedo et al., 2017	Retrospective cohort study	Pregnant and postpartum women (up to 42 days) admitted into the ICU (n = 702) due to direct and indirect obstetric causes.	ICNARC obstetric EWS	Death	AUROC 0.84 (AUROC of 0.87 in direct and 0.77 in indirect obstetric admissions)
Nathan HL et al., 2017	Prospective cohort	Women with preeclampsia at admission (n = 1547)	CRADLE Vital Signs alert EWS	Kidney injury, MgSO4 use, and ICU admission, death	Trigger predicted an increased risk of Kidney injury (OR 1.74), MgSO4 use (OR 3.4) and ICU admission (OR 1.5)
Theme 2	Studies testing the effectiveness of EWS in improving measured outcomes in an obstetric population				
Publication	**Design**	**Participants**	**EWS**	**Outcomes**	**Findings**
Austin DM et al., 2013	Mixed retrospective (before) and prospective (after) design	Retrospective (n = 42) and prospective (n = 71) obstetric admissions	EWS	Severity of morbidity	MDT review determined that EWS might have reduced severity of morbidity, by 7.6%
Maguire PJ et al., 2015	Mixed retrospective (before) and prospective (after) design	Obstetric patients with bacteraemia before (n = 61) and after (n = 20) IMEWS	IMEWS	Vital signs recording and trigger/antibiotic time lag	Improvement in RR recording ($p<0.05$) and reduction in time between trigger and antibiotics ($p>0.05$)
Maguire PJ, 2016	Retrospective observational study	Women monitored with IMEWS (n = 80) and other methods (n = 87) before ICU admission	IMEWS	ICU Admission	IMEWS contributed to early recognition of critical illness (in 73.8% of participants, n = 80) but cannot replace clinical judgment

(*Continued*)

Table 1. (Continued)

Shields E L et al. 2016	Quasi-experimental	Obstetric admissions in 6 hospitals n = 11399	MEWT	CDC defined maternal morbidity, ICU admission	Reduction in morbidity (p = 0.01) and ICU admission (p = 0.8)
Sheikh S et al., 2017	Before after Quasi-experimental	Women who had CS before (n = 100) and after (n = 100) implementation of NEWS	NEWS	Need for specialist review, ICU admission, referral due to post-op complications, death	No statistically significant difference
Merriel A et al., 2017	Before after Quasi-experimental	Women undergoing CS before (n = 79) and after (n = 85) implementation	MEOWS	Pre-operative stabilization, action taken due to trigger	Significant improvement in the two outcomes (p<0.05). pre-op stabilization improved after MEOWS: odds ratio 2.78, 95% CI, 1.39–5.54. Improved care triggered in 68% of patients after EWS compared to 4% before (p<0.001)

AUROC: Area Under Receiver Operating Characteristic Curve, **EWS**: Early Warning Systems, **ICU**: Intensive Care Unit, **IMEWS**: Irish Maternity Early Warning System, **MEOWS**: Modified Early Obstetric Warning Systems, **MEWT**: Maternal Early Warning Triggers, **NEWS**: National Early Warning System, **NPV**: Negative Predictive Value, **PPV**: Positive Predictive Value

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modified for obstetric populations. [5,26] The other two [14,15] used statistically derived EWS generated from multi-country prospective cohort studies designed for use in pre-eclampsia patients only. The resulting EWS included vital signs, laboratory investigations, and clinical signs, and may not be applicable to all obstetric patients or in low resource settings.

Diagnostic accuracy of EWS

Seven of the 11 included studies that tested the effectiveness of EWS in predicting obstetric morbidity/mortality had death as a primary outcome Table 1.

Accuracy in predicting maternal death. Two studies were retrospective, of good or moderate quality (Appendix C in S1 Table) and were on all obstetric patients admitted to intensive care units. Both studies showed that the obstetric EWS had a very high accuracy in predicting death (AUROC >0.80) among critically ill obstetric patients [9,16].

Five studies on specific obstetric populations had a high risk of bias or concern for applicability Appendix B2 in S1 Table [5,15,17,18,21]. Three of these were large prospective studies that focused on women with pre-eclampsia and reported high sensitivity (>85%), specificity (>75%) and AUROC (>0.75) of EWS in predicting death. [15,17,18] Two retrospective

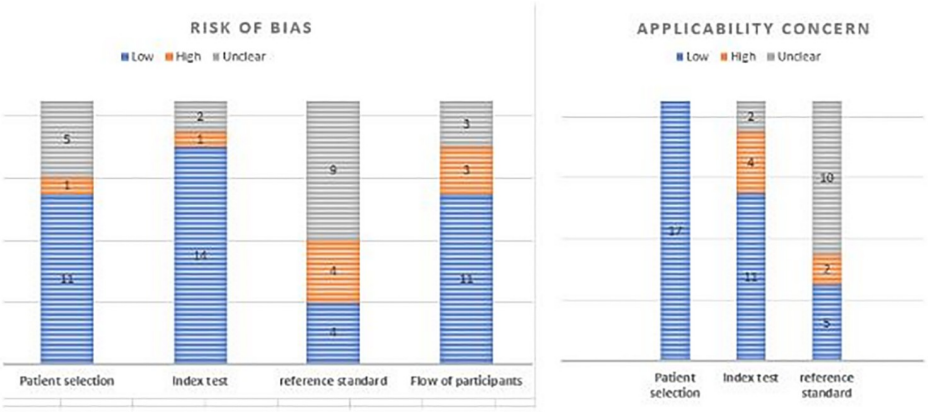

Fig 3. Quality assessment of included studies (n = 17).

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studies with pregnancy-related sepsis only population, showed that EWS did not accurately predict death (PPV <10%, AUROC < 0.75) [5,21].

Accuracy in predicting morbidity and ICU admission. Five studies [5,17,20,22,23] reported the accuracy of obstetric EWS in predicting increasing severity of obstetric morbidity or ICU admission. General obstetric study populations were used in three of these studies. [20,22,23] Although these studies were of varying quality, they reported that EWS had a very high median (inter-quartile range) sensitivity of 89% (72% to 97%) and specificity of 85% (67% to 98%). The median (inter-quartile range) positive predictive values were low—41% (25% to 74%) Table 1.

Two retrospective studies reported very poor predictive accuracy (PPV less than 10% and AUROC of less than 0.75) of obstetric EWS for severe sepsis among cohorts of women with chorioamnionitis. [5,21] Table 1. However, the dataset used in the two studies had a high risk of attrition bias as more than 50% of the participants had incomplete vital signs records and were excluded from the analysis; Appendix C in S1 Table.

The effectiveness of EWS in improving clinical outcomes

Six studies [22,24–27,29]assessed the effectiveness of EWS in improving outcomes in general obstetric populations. The outcome measures included clinical outcomes (morbidity, maternal death, and ICU admission) and trigger system measures (vital sign recording, the time lag between the trigger and corrective clinical action, preoperative stabilization, need for specialist review and referral rate) Table 2.

Maternal morbidity, death and ICU admission. Only one before and after study in patients who had had a caesarean section had maternal death as an outcome measure [26]. In that study, the two periods (pre and post-EWS implementation) compared were not equal, it was unclear if the sample was large enough to detect any difference in the outcome. However, there was a significant reduction in complications due to post-partum haemorrhage (PPH) after EWS introduction (Table 1). The reduction in PPH after the introduction of the EWS compared to before was attributed to early recognition and timely management.

In a large quasi-experimental study there was a significant reduction in CDC-defined severe and composite maternal morbidity ($p<0.01$) but not mortality in 6 intervention hospitals following EWS implementation, compared to 19 control hospitals. Also, there was no change in the ICU admission rate in the intervention and control hospitals [22].

There was a non-significant reduction in ICU admission and severity of obstetric morbidity after implementation of EWS in two before and after studies [24,29] Table 1.

Table 2. Outcomes assessed by the EWS effectiveness studies (n = 6).

	Outcome measures						
Publication	**Morbidity**	**ICU admission**	**Maternal Death**	**Vital sign recording**	**Time lag***	**Preop stabilization****	**Referral rate#**
Austin DM et al., 2013	✓						
Maguire PJ et al., 2015				✓	✓		
Maguire PJ et al., 2016		✓					
Shields E L et al. 2016	✓	✓					
Sheikh S et al., 2017		✓	✓				✓
Merriel A et al., 2017						✓	

*Time lag: time interval between trigger and review.

**Preop stabilization: clinical actions taken to optimize patients undergoing a caesarean section.

Referral rate: rate of referral of sick patients to a higher level of care, including critical/intensive care

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Quality of patient care. One before-after study (before n = 61, after n = 20) reported an increase in the frequency of documentation of vital signs (specifically for respiratory rate) following the implementation of the Irish Maternity Early Warning System [25]. The authors also reported a statistically significant reduction in the time interval between EWS trigger and antibiotic administration for obstetric patients with bacteraemia.

Pre-operative stabilization of women undergoing caesarean section was reported to have significantly improved after implementation of EWS (Odds ratio 2.78, 95% CI, 1.39–5.54) [27]. Also, there were improvements in care triggered by abnormal EWS observations in 68% of patients after EWS implementation compared to only 4% before ($p<0.001$).

In another before-after study (before n = 100, after n = 100), Sheikh and colleagues [26] reported a non-statistically significant reduction in the need for specialist review. Similarly, there was a non-significant higher-level referral rate due to post-operative complications among women who had a caesarean section, after implementation of EWS.

EWS parameters

Details of 16 versions of EWS were identified from the reviewed studies. The components of the EWS used in one study was not specified [26]. There were variations in parameters included among the reviewed EWS charts; however, 14 of the 16 charts had pulse rate, systolic blood pressure, and respiratory rate, 13 charts had temperature and 12 charts had diastolic blood pressure and conscious level. On average four in five charts identified in this review (mean, 82.5%; n = 16) had these 5 parameters.

Discussion

Our systematic review did not identify any randomised controlled trials on EWS. It included 17 studies, mostly observational studies [11] and only two of all included studies were conducted in low-income countries. All studies that assessed the predictive accuracy of EWS for adverse obstetric outcomes were observational studies. Most of the studies that assessed the effectiveness of EWS in improving clinical outcomes were of quasi-experimental design.

For a screening tool to be of value, it should be safe to use, cost effective, accurate and acceptable to care, providers. The accuracy of an early warning chart to predict morbidity is indicated by the positive or negative predictive value (PPV/NPV). Both of these are dependent on the prevalence of the condition. While it is desirable that a screening test should have a high sensitivity and specificity, the probability of a positive result when the condition actually exists (PPV) or the probability of a negative result when the condition does not exist (NPV) is equally important. A screening tool for a condition of low prevalence, with high sensitivity and specificity, will likely have a low PPV and a high NPV. While for more common conditions, a screening test/tool with similar sensitivity and specificity will likely have a high PPV and a low NPV.

Early warning systems developed using a statistically derived model for obstetric population admitted to the critical care unit are accurate in predicting death (AUROC >0.80) [16]. In other general obstetric population, EWS haswas shown to be highly sensitive and specific in predicting morbidity and ICU admission, with comparatively low PPV (average of 41%). With a low probability that subjects with a positive screening test are truly at risk of deterioration (low PPV), there is the risk of unnecessary use of resources when protocols are triggered due to a 'positive' test. Similarly, EWS with low NPV may miss many women who are likely to deteriorate clinically by giving them a false resuarrance, and potentially resulting in catastrophic outcomes.

One low quality multicentre controlled trial reported that obstetric EWS significantly reduces CDC-defined maternal morbidity but not ICU admission rate [22]. A reduction in ICU admission will have been expected because the implementation of corrective measures may reduce the need for ICU admission however the management of women who are predicted to develop morbidity may be best in the ICU. Therefore ICU admission rate may not be a good outcome measure because the criteria for ICU admission may vary.

The low positive predictive values for severe morbidity and ICU admission (PPV 41%) means that approximately, only one in two cases with a positive screening test is truly at risk of deterioration. As pointed out by Friedman, [30] a warning system with a high false-positive rate, may potentially worsen clinical care, constitute a nuisance alarm and contribute to alarm fatigue.

However, the relatively low positive predictive value for obstetric morbidity and ICU admissions reported in this review is comparable to other non-obstetric aggregated and single parameter early warning systems [31,32]. Hence, as with these non-obstetric EWS, and as pointed out by Maguire and colleagues, [29] obstetric EWS needs to be used with, and do not substitute, clinical judgment in patient monitoring and care.

Based on one small sample low-quality quasi-experimental study, there is no evidence that EWS reduces maternal deaths [26].

There is some evidence from small sample size, low-quality studies that introduction of EWS improves the quality of care for obstetric patients. Specifically, EWS significantly improves the frequency of vital sign observation, and improves pre-caesarean section stabilization of patients [26,27]. Also Maguire et al. in a small sample before after study, reported that EWS reduces the time interval between abnormal vital signs and implementation of corrective clinical action but this was not statistically significant.[25]

There are some conflicting findings, particularly on the use of EWS in women with chorioamnionitis. Lappen et al.[5] and Edwards and colleagues [21] reported very poor performance for predicting sepsis in women with chorioamnionitis and argued that the EWS should not be used in this population. However, the findings were not surprising because information of vital signs was missing from records of 549 of the 913 women and was excluded from the analysis [21,28]. For this reason, we assessed the two studies as having a high risk of attrition bias; Appendix C in S1 Table.

Fourteen of the 16 EWS versions identified in this review included five parameters; the pulse rate, respiratory rate, temperature, blood pressure, and consciousness level. These parameters need simple patient monitoring devices that are readily accessible (BP machine, a thermometer, and a clock or timer) to measure. This finding suggests that EWS may be feasible to implement in low-resource settings where more sophisticated monitoring and diagnostic equipment may be unavailable [33]. However, evidence from a prospective cohort study identified the need for local validation and impact assessment of EWS tools before their adoption in resource-limited settings [34].

This systematic review provides more information than the previous systematic review in 2013 [8], on the predictive accuracy and effectiveness of obstetric EWS. Our results support the hypothesis that EWS may improve the quality of monitoring of obstetric patients, possibly resulting in improved reaction time by clinical staff to prevent further deterioration. These findings agree with outcome improvement reported with EWS in non-obstetric patients population [32].

To the best of our knowledge, this is the first systematic review to report predictive accuracy, and effectiveness on clinical outcomes of obstetric EWS. Other strengths of this review include adherence to the good practice of protocol registration and use of a robust tool for quality assessment in diagnostic accuracy studies. A limitation of our review is the lack of

standardization of the defining criteria for outcomes. For instance, maternal morbidity was defined based on the CDC-criteria in the study by Shields et al., [22] while other studies [4,19,24] defined morbidity based on consensus among authors. We, therefore, identified a need to standardize outcomes in EWS effectiveness studies for clinical and research purposes. Most of the studies included were observational studies and only one of the studies that assessed the effectiveness of EWS in improving clinical outcomes had death as a primary outcome. More robust studies with large sample sizes are required to detect the effect of EWS on maternal deaths.

There were different versions of obstetric EWS across hospitals in keeping with lack of standardization as reported for non-obstetric systems. [32] This can result in a lack of familiarity with local systems when staff move between clinical areas and hospitals.

Finally, the 12 EWS validation studies revealed a strong association between high scores and adverse obstetric outcomes. However, only one study assessed the time interval between the EWS trigger across different parameters and intravenous antibiotic administration [29]. Robust studies, for example, cluster randomised controlled trials, with the interval between a trigger and corrective clinical action as an outcome measure, are needed.

Conclusion

Obstetric EWS are highly sensitive and specific in predicting obstetric morbidity and ICU admission with relatively low, but comparatively acceptable PPV. This supports their utility as valuable bedside screening tools for morbidity among the general obstetric population. Early warning systems are highly accurate in predicting maternal death among critically ill obstetric patients, but there is limited evidence of their effectiveness in reducing maternal deaths. Obstetric EWS may improve the frequency of routine vital sign observation and may reduce the interval between patient deterioration and corrective clinical action. These can potentially improve the quality of care for pregnant/postpartum women and reduce the risk of adverse obstetric outcomes. Most obstetric EWS versions have basic clinical observations that can be routinely collected in resource-limited settings making them feasible for use in such settings. More robust studies are however needed to assess the effectiveness of obstetric EWS in reducing maternal deaths.

Supporting information

S1 Table. Appendix A-C (A-combination of serch terms, B1-quality assessment tool, B2-QUADA 2 scoring guideline, C-quality of individual studies).
(PDF)

S2 Table. PRISMA check list.
(DOC)

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Author Contributions

Conceptualization: Aminu Umar, Charles A. Ameh, Matthews Mathai.

Data curation: Aminu Umar, Francis Muriithi.

Formal analysis: Aminu Umar, Charles A. Ameh, Francis Muriithi.

Funding acquisition: Charles A. Ameh.

Investigation: Charles A. Ameh.

Methodology: Aminu Umar, Charles A. Ameh, Matthews Mathai.

Project administration: Charles A. Ameh.

Resources: Charles A. Ameh.

Supervision: Charles A. Ameh, Matthews Mathai.

Validation: Charles A. Ameh, Matthews Mathai.

Writing – original draft: Aminu Umar, Charles A. Ameh.

Writing – review & editing: Charles A. Ameh, Francis Muriithi, Matthews Mathai.

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Annex 9

Development and Validation of Obstetric Early Warning System model for use in low resource settings

Aminu Umar MPH[1]
Alexander Manu PhD[1]
Matthews Mathai PhD[1]
Charles Ameh[1] PhD
[1]Centre for Maternal and Newborn Health, Department of International Public Health, Liverpool School of Tropical Medicine, United Kingdom

Corresponding author: Charles.Ameh@lstmed.ac.uk, +447714753844

Abstract

Introduction

The use of obstetric early-warning-system (EWS) has been recommended to improve timely recognition, treatment and early referral of women who have or are developing a critical illness. The development of such diagnostic prediction models should involve a statistical combination of predictor clinical observations into a multivariable model which should be validated. No obstetric EWS has been developed and validated for a low resource setting. We report on the development and validation of a simple obstetric diagnostic prediction EWS model for resource-limited settings.

Methods

We performed a multivariate logistic regression analysis using a retrospective case-control study design with clinical indices predictive of severe maternal outcome (SMO). Cases were 4360 women diagnosed with SMO in 42 Nigerian tertiary-hospitals between June 2012 and mid-August 2013. Matched controls were 1000 obstetric admissions without SMO diagnosis. We used clinical observations collected within 24 hours of the occurrence of SMO. We created a combined dataset with two controls per case, split randomly into development (n=600) and validation (n=600) datasets. We assessed the model's validity using sensitivity and specificity measures and its overall performance in predicting SMO using receiver operator characteristic (ROC) curves. We then fitted the final derived model on the validation dataset and assessed its performance. Using the reference range proposed in the United Kingdom Confidential-Enquiry-into-Maternal-and-Child-Health 2007-report, we converted the model into a simple score-based EWS.

Results

The final model comprised abnormal systolic blood pressure-(SBP>140mm Hg or <90mmHg), high diastolic blood pressure-(DBP>90mmHg), respiratory rate-(RR>40/min), temperature-(>38^{o}C), pulse rate-(PR>120/min), caesarean-birth, and the number of previous caesarean-births. The model was 86%-(95% CI 81-90) sensitive and 92%- (95% CI 89-94) specific in predicting SMO with area under ROC of 0·92-(95% CI 0·90 – 0·95). All parameters were significant in validation models except DBP. The model maintained good discriminatory power across all validation data sets (AUC>90%) and had good screening characteristics

Conclusion

We developed an obstetric EWS with (RR, temperature, SBP, pulse rate, consciousness level, urine output and delivery mode, that performed well in predicting SMO in a low-resource setting.

keywords
Obstetric early warning system, diagnostic predictive model, low-resource settings.

Funding
None

Summary box

What is already known?

- Obstetric early warning systems (EWS) have a very high median (inter-quantile range) sensitivity 89% (72% to 97%) and specificity 85% (67% to 98%) but low median (inter-quantile range) positive predictive values, 41% (25% to 74%) for predicting morbidity or ICU admission.
- Obstetric EWS are highly accurate in predicting death (AUROC >0.80), improves the frequency of routine vital sign observation and reduces the interval between EWS trigger and corrective clinical action.
- Fourteen of the 16 EWS identified in a recent systematic review, used basic clinical observations such as systolic and diastolic blood pressure, pulse rate, temperate, and respiratory rate, all easily collected in low resource settings.
- There is no statistically derived and validated obstetric EWS for low resource settings.

What are the new findings?

- An obstetric early warning system was developed and internally validated based on Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis statement.
- The predictive model comprised abnormal systolic blood pressure (SBP>140mm Hg or <90mmHg), high diastolic blood pressure (>90mmHg), respiratory rate (RR>40/min), temperature (>38^{o}C), pulse rate (PR>120/min), caesarean birth, and the number of previous caesarean births.
- The model was 86% (95% CI 81-90) sensitive and 92% (95% CI 89-94) specific in predicting SMO with area under ROC (AUC) of 0·92 (95% CI 0·90 – 0·95).
- The model maintained good discriminatory power across all validation data sets (AUC>90%) and had good screening characteristics

What do the new findings imply?

- The obstetric EWS developed may be effective in predicting severe maternal outcomes in low-resource setting.

Introduction

The World Health Organization (WHO) estimated that 303, 000 maternal deaths occurred globally at the end of the Millennium Development Goals (MDGs) in 2015. Over 99% of these deaths occurred in low and middle-income countries (LMICs), most of which made insufficient progress towards achieving the MDG maternal health targets [1]. It is also estimated that there are 27 million episodes of direct obstetric complications annually which contribute to long-term pregnancy and childbirth complications [2]. Following increasing access to facility-based births, partly because of Universal Health Coverage policies under the Sustainable Development Goals since 2016, opportunities to ensure good quality facility care are critical, if the new ambitious global and national Maternal Mortality Ratio (MMR) targets are to be achieved [3].

The increased burden of adverse outcomes, especially in LMICs is believed to be due primarily to delays in the recognition of pregnancy complications [4,5]. Early warning systems (EWS) are clinical diagnostic prediction models that involve serial clinical observations ("track") with criteria ("trigger") to identify patients at risk of complications [6]. A 2018 systematic review of EWS used in obstetrics found that they are effective in predicting adverse obstetric outcomes and reducing obstetric morbidity [7]. The United Kingdom Confidential Enquiry into Maternal and Child Health (CEMACH) (2003-2005 report) recommended "the use of obstetric EWS to improve timely recognition, treatment and referral of women who have or are developing a critical illness" [8]. Most of the available obstetric EWS versions used subsequently were designed based on clinical consensus rather than the application of recommended prediction model development methodology that should include statistical analysis of outcome measures [9–17].

Model development involves a statistical combination of predictor clinical observations into a multivariable model. The Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement recommends that new prediction models are tested on data used in its development (internal validation) and other data not used (external validation) [10].
In 2013, the first statistically derived, obstetric EWS was developed and internally validated using clinical observations (physiological variables) collected from 4400 women during their first 24 hours of critical care admission [18]. The EWS developed showed a good predictive ability to discriminate survivors from non-survivors in the derivation dataset, and on an external dataset [19]. However, since the database used in the development, internal [18] and external validation [19] of the EWS were only for women admitted to critical care, the EWS may not be suitable for an obstetric population without the obvious need for critical care and other settings.

No obstetric EWS has been developed and validated for a low resource setting. However, 14 of the 16 obstetric EWS identified in a recent systematic review, had five clinical observations/physiologic variables (pulse rate, systolic blood/diastolic pressure, respiratory rate, temperature and conscious level) [7] that can be easily collected even in low resource settings.

We report on the development and validation of a simple obstetric diagnostic prediction model and EWS for use in resource-limited settings.

Methods

Study design

The study was a retrospective (case-control) analysis of secondary data on admissions to inpatient obstetric wards in Nigerian tertiary hospitals. Cases based on standardised definitions were derived from the Nigerian near-miss study, the largest prospective investigation of maternal deaths and near-misses in Africa, [20]. Controls were women who were admitted for obstetric care at the same time as the cases. These admissions took place between June 2012 and August 2013.

Study Population and Data Sources

The study protocol and findings of the Nigerian Near-miss study have been published elsewhere [20,21]. All women admitted to 42 Nigerian tertiary hospitals for birth or within 42 days of birth/termination of pregnancy between June 2012 and August 2013 were eligible for enrolment into the study. The study reported severe maternal outcome (SMO) cases based on the World Health Organization (WHO) near-miss criteria (organ dysfunction, clinical and management-based) [20,22]. We included data from all 4360 women who had SMO during the 14-month surveillance.- of these women 998 died and 3362 were near-miss cases [22]. One thousand women who were admitted to three of the 42 hospitals for birth and discharged with no SMO were the controls. All data were collected within 24 hours of the occurrence of SMO (for cases) or 24 hours of birth/end of pregnancy (collected retrospectively for controls).

Data abstraction

Individual-level data on all study variables were abstracted from the Near-miss study dataset (n=4360) and from the case notes of 1000 controls. These included demographic characteristics (age, weight, height), obstetric variables (parity, the number of antenatal clinic visits, gestational age at time of admission/delivery, delivery mode, interval from last pregnancy, the number of previous caesarean section), diagnosis, length of stay in hospital, and the last haematocrit measured. Abnormal clinical indices were extracted from the cases dataset based on their definitions codebook including high (>140 mm Hg) and low (<90 mm Hg) systolic blood pressure, high (>90 mm Hg) and low (<60 mm Hg) diastolic blood pressure, high (>38°C) and low (<35°C) temperature, marked tachycardia

(PR>120/min) and bradycardia (PR<60/min), hypoxaemia (SpO_2<90%), severe tachypnoea (RR>40/min) and bradypnea (RR<6/min), severe oliguria (urine output<300 mL in 24 hours), and coma (Glasgow Coma Score<8/15). Among the controls, the data were collected as continuous variables and classified based on the cut-off values in the cases dataset codebook.

Outcome

The outcome measure for this analysis was SMO, computed as the sum of maternal deaths and near-misses and transformed into a binary variable-occurred or not. Maternal death was defined according to the International Classification of Diseases (ICD-10) [23]. Women were identified as a maternal near-miss if they met any of the three near-miss criteria (clinical criteria related to a specific disease entity, intervention-based criteria and organ system dysfunction-based criteria) [22].

Statistical methods

The characteristics of the study population were summarised by means and standard deviations for continuous and percentages for categorical variables. Continuous variables were compared between cases and controls through analysis of variance or Kruskal-Wallis Tests, depending on whether or not variables were normally distributed. Normality was assessed visually through distribution plots and with the Shapiro-Wilk test. Data for 1200 study participants were randomly sampled from the combined dataset and randomly allocated into the development dataset (n=600) or validation data set (n=600) with two controls per case. This sample size estimate was based on a baseline SMO prevalence of 4·8%. At 5% level of significance, the analysis could detect an absolute difference in SMO prevalence of 6% and 5% at 90% and 80% powers, respectively.

Model building

Univariable logistic regression models were fitted to assess the association between each predictor variable and outcome (SMO), in turns. A stricter inclusion criterion was applied and therefore variables were only selected from the univariable models for inclusion into the multivariable model if the model p-value<0·05. This yielded 22 potential factors for inclusion.

Multivariable logistic regression models were fitted using the backward stepwise approach and factors were removed from the model one at a time based on the highest p-value>0·05 and their Likelihood ratio. When the final model was achieved, a sensitivity test was performed by including each of the eliminated variables, in turn, into the final model to assess their significance. None of these was found significant in the final model. One variable was dropped from the model for collinearity with other variables. We verified the collinearity by a simple check of the correlation between the suggested variables.

Model performance

Performance of the obstetric EWS clinical prediction model from the derivation data set was tested on the two validation data sets [24]. First, the overall validity (sensitivity, specificity, negative predictive value-NPV and positive predictive value-PPV), as well as the area under the curve (AUC) for the Receiver Operating Characteristics (ROC) curves, were assessed for the final model. Discrimination was assessed using the *c* statistic or AUC, an estimate of the probability of assigning a higher risk to those who suffered an SMO compared to those who did not. The final model was then applied to the validation dataset, and the performance was similarly assessed. Finally, we estimated the validity of the selected EWS predictors by applying the final model to the entire (n=5243 after excluding missing data) dataset of cases and control, bearing in mind that the ratio of cases to controls had been reversed – over 4 cases per control. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 25 and Stata version 15·1. We constructed 95% confidence intervals (95% CI) for all performance characteristics.

Obstetric EWS monitoring chart

Our statistically derived diagnostic prediction model was modified based on the clinical importance of rejected variables. Given that the cases data set provided categorised (binary) clinical variables, it was not feasible to validate reference ranges for the different model parameters. Hence, the final modified obstetric early warning system model was converted into simple score-based monitoring chart using the reference range proposed in the MEOWS chart recommended in the 2007 CEMACH report [8] (Supplementary document: Appendix 1).

Patient and Public Involvement statement

Patients were not involved in development of the research question or design of this study. Secondary patient monitoring data was used for this analysis. Implications of this study will be disseminated through patient groups and blogs in the study setting.

Ethical considerations

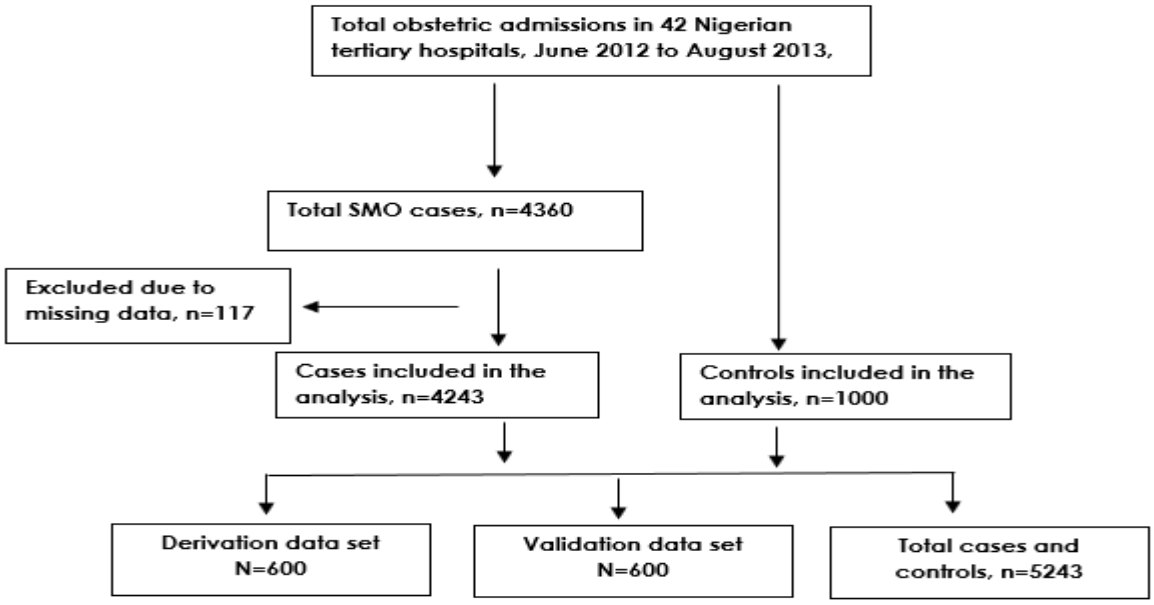
Clearance was obtained from the principal investigators of the Nigerian Near-Miss study (from the WHO, Geneva, Switzerland) for the use of the data. A data use agreement was signed in which the PIs indicated that this analysis was covered under the approved use of data by the Ethics Review Committee at the WHO and all 42 participating hospitals. However, additional approval for this study was obtained from the Research Ethics Committee of the Liverpool School of Tropical Medicine (Protocol ID 17-047).

We present our findings according to the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis statement[10].

Results

From the 100,107 women admitted for pregnancy, childbirth or puerperal complications during the 14-month period of the Nigerian near-miss study, 4360 developed SMO and their data were included in the cases data set. Of these, 998 women died and 3362 suffered maternal near-miss. A total of 117 (2·7%) women with SMO had missing data, with no records of the type of SMO (death or near-miss) they experienced. These women were excluded from the analyses as the missingness was assumed to be completely at random. The lack of data on other characteristics of these participants did not allow for assessment of bias in dropping them from the analysis. None of the control participants had missing parameters. Figure 1 illustrates allocation into, and composition of, the development and validation data sets.

Figure 1: Creation of the development and validation data sets



Characteristics of the SMO cases and the controls are given in Table 1. Those who experienced SMO tended to be older and more likely to be obese. They also stayed longer in hospital, with the mean number of days on admission four times greater than the controls and were more likely to be anaemic. There was no significant difference in terms of parity, but SMO cases had more preterm births and had a significantly shorter duration from last pregnancy.

Table 1: Characteristics of severe maternal outcome cases (n=4243) compared with controls who were discharged after normal vaginal birth (n=1000)

Variable	SMO cases	Controls	P-Value
Age at baseline, mean (SD)	27·8 (6·5)	26·8 (6·1)	<0·001
Weight on admission, mean (SD)	75·7 (14·9)	67·2 (13·9)	0·002
Height in meters, mean (SD)	1·6 (0·1)	1·6 (0·3)	<0·001
Days on admission, mean (SD)	6·8 (5·2)	1·6 (0·7)	0·040
Number of ANC Visits, mean (SD)	4·6 (3·5)	3·6 (2·9)	<0·001
Last PCV, mean (SD)	27·6 (9·8)	33·3 (5·9)	<0·001
Parity, mean (SD)	4·5 (2·0)	4·4 (1·0)	>0·050
Gestational age in weeks, mean (SD)	35·8 (4·5)	38·4 (4·7)	<0·001
Months since last birth, mean (SD)	3·3 (18·9)	44·8 (13·9)	<0·001

Overall, women who had abnormal clinical observation measurements (either lower or higher than normal), based on the pre-defined cut-off points deciphered from the cases dataset, were more likely to develop SMO than the controls (Table 2). Initially, bivariate analysis was performed considering all 22 potential variables for entry in the model. Of these, a total of 15 had a significant p-value (<0·05) (Table 2), and so these were considered for potential inclusion in the multiple regression model.

Table 2: Statistically significant clinical variable from univariate analysis (dependent variable; SMO binary outcome variable)

Parameters	Cases N=200	Controls N=400	Chi-square significance
High systolic blood pressure (>140), ***number (%)***	75 (68·8)	34 (31·2)	<0·001
Low systolic blood pressure (<90), ***number (%)***	58 (61·7)	36 (38·3)	<0·001
High diastolic blood pressure (>90), ***number (%)***	75 (64·7)	41 (35·3)	<0·001
Low diastolic blood pressure (<60), ***number (%)***	110(65·5)	58 (34·5)	<0·001
Severe tachypnoea (RR>40), ***number (%)***	26 (92·9)	2 (7·1)	<0·001
Severe bradypnea (RR<6), ***number (%)***	5 (100)	0 (0)	<0·001
Fever (Temp>38), ***number (%)***	17 (94·4)	1 (5·6)	<0·001
Marked tachycardia (PR>120), ***number (%)***	58 (71·6)	23 (28·4)	<0·001
Hypoxaemia (SP02<90%), ***number (%)***	14 (82·4)	3 (17·6)	<0·001
Caesarean delivery in present admission, ***number (%)***	51 (94.4)	3 (5·6)	0·001
Low urine output (300ml/24hours), ***number (%)***	12 (100)	0 (0)	<0·001
Prolonged unconsciousness (GCS<8/15), ***number (%)***	14 (100)	0 (0)	<0·001
Blood transfusion in present admission, ***number (%)***	40 (67·8)	19 (32·8)	0·038
Last haematocrit level, ***mean (SD)***	27·6 (9·8)	33·3 (5·9)	<0·001
Days on admission, ***mean (SD)***	6·8 (5·2)	1·6 (0·7)	0·040

The significant variables were entered into a multiple logistic regression model. Both backward and forward stepwise selection methods were used to build the final parsimonious model, with the standard 5% significance level for entry and removal. Both techniques produced the same final model, in five steps, with 8 parameters (high systolic blood pressure (>140 mm Hg), low systolic blood pressure (<90 mm Hg), high diastolic blood pressure (>90 mm Hg), severe tachypnoea (RR>40/min), fever (temperature >38^{o} C), marked tachycardia (PR>120/min), delivery mode (caesarean or vaginal birth), and the number of previous caesarean births).

Risk of severe maternal outcome

Table 3 gives the odds ratios of developing SMO for the variables in the final model. The risk of developing SMO was five times greater among women with high systolic blood pressure (>140 mm Hg) and tachycardia (PR>120/min), while low systolic BP (<90 mm Hg) increased SMO risk by four times. Caesarean delivery during index admission was found to increase risk of SMO significantly (absolute risk of six), but the number of previous caesarean sections according to the model did not increase risk. Most importantly, the variables with the highest risk of SMO in the model were fever and tachypnoea, with absolute risks of 117 and 25, respectively.

Table 3: Results of multiple logistic regression analysis using significant predictor variables (n=15) from the univariate analysis: Outcome variable is SMO

Development Model (n=600)						
Parameters	**Odd ratio**	**S. E**	**Significance (p)**	**95% CI**		**Absolute risk***
				Lower	**Upper**	
sBP>140 mmHg	5·26	0·49	0·001	2·03	13·63	5
sBP<90 mmHg	3·73	0·42	0·002	1·65	8·41	4
dBP>90 mmHg	2·78	0·48	0·035	1·08	7·16	3
RR>40 cycles/min.	25·20	0·92	<0·001	4·19	51·60	25
Temp>38^{0}C	116·51	1·12	<0·001	12·96	147·42	117
PR>120/min	4·62	0·43	<0·001	2·00	10·66	5
CS (Yes vs No)	5·91	0·38	<0·001	2·79	12·53	6
Number of CS	0·96	0·01	<0·001	0·95	0·97	1
Validation model (n=600)						
Parameters	**Odd ratio**	**S. E**	**Significance (p)**	**95% CI**		**Absolute risk***
				Lower	**Upper**	
sBP >140 mmHg	10·01	0·67	<0·001	2·72	36·88	10
sBP < 90 mmHg	3·40	0·39	0·002	1·57	7·36	3
dBP > 90 mmHg	2·70	0·65	0·129	0·75	9·70	3
Temp>38^{0}C	18·21	0·95	0·002	2·83	116·95	18
PR>120/min	125·01	1·10	<0·001	14·43	108·31	125
CS (yes vs no)	5·85	0·42	<0·001	2·59	13·19	6
Number of CS	0·98	0·06	<0·001	0·97	0·99	1
PR>120/min	4·14	0·40	<0·001	1·89	9·08	4
Validation model with total data set (n=5243)						
Parameters	**Odd ratio**	**S. E**	**Significance (p)**	**95% CI**		**Absolute risk***
				Lower	**Upper**	
sBP >140 mmHg	15·50	0·31	<0·001	8·38	28·69	16
sBP < 90 mmHg	2·09	0·20	<0·001	1·42	3·08	2
dBP > 90 mmHg	0·89	0·30	0·706	0·50	1·61	1
RR > 40 cycles/min	23·19	0·47	<0·001	9·18	58·57	23
Temp > 38^{0}C	55·90	0·46	<0·001	22·64	138·02	56
CS (yes vs no)	6·38	0·16	<0·001	4·71	8·65	6

Number of CS	0·98	0·00	<0·001	0·98	0·98	1
PR > 120	6·27	0·21	<0·001	4·14	9·50	6

*Absolute risk estimated by rounding the odds ratios to one significant figure

Although significant in the derivation model, high diastolic pressure (>90mmHg) was not as much of a risk factor as the systolic BP, and thus ceased to have a significant effect on SMO risk in the two validation datasets (Table 3). When interactions were considered, the diastolic blood pressure was found to be strongly collinear (correlation coefficient, r = 0·95) with systolic blood pressure, therefore diastolic BP was dropped in the proposed EWS monitoring chart (Supplementary file: Appendix 2). When applied in the validation data sets, all other variables in the original model produced a consistent effect in the same direction with variation in effect sizes (Table 3). Similarly, the clinical variables with the highest risk of SMO in the two validation models were fever and tachypnoea, with absolute risks of 125 and 18 respectively in the first validation model, and 56 and 23 respectively in the validation model with the complete case and control data.

Predictive accuracy for SMO

The final early warning system model from the derivation data set explained 66% of the variability in SMO with area under receiver operator characteristic curve of 92% (Table 4, Supplementary file: Appendix 3). Given that the cases data set provides an already categorised (binary) clinical variables, the diagnostic accuracy of the models was assessed based on the number of parameters required to predict SMO with best screening properties. Using presence of five or more triggers as the cut-off point to define SMO, the model predicted SMO with a sensitivity of 86%, a specificity of 92%, positive and negative predictive values of 84% and 93% respectively (Table 4). The first validation model produced very similar screening characteristic and discriminatory ability (AUROC 92%) Table 4, Supplementary file: Appendix 4. Not surprisingly, however, the model with all cases and controls produced the highest positive predictive value (94%), but significantly reduced the negative predictive value (61%). This is expected given the high prevalence of the outcome measure in the data set (case: control = 4:1). The model explained 58% of the variability in SMO with 92% discriminatory ability (AUROC 82%) Table 4, Supplementary file: Appendix 5).

Table 4: Predictive accuracy of the early warning system models (best performing cut-off 0.6)

Model	Sensitivity (%) (95%, CI)	Specificity (%) (95%, CI)	PPV (%) (95%, CI)	NPV (%) (95%, CI)	AUROC (95%, CI)	Negelkerke R^2
Original model (n=600)	86 (81-90)	92 (89-94)	84 (79-89)	93 (90-95)	0·92 (0·90-0·95)	0·69
Internal validation 1 (n=600)	81 (76-86)	90 (87-93)	81 (75-85)	90 (87-93)	0·92 (0·88-0·94)	0·69
Internal validation 2 (n=5243)	91 (90-92)	71 (68-74)	94 (93-95)	61 (58-64)	0·92 (0·90-0·95)	0·58

Proposed EWS chart

Measurements of temperature, pulse rate, systolic blood pressure, respiratory rate and delivery mode, in postpartum patients (caesarean delivery versus spontaneous vaginal delivery), constitute the primary early warning parameters from the three statistical models. Diastolic blood pressure was dropped as it was strongly collinear with systolic blood pressure (r = 0·95), and the latter was more clinically relevant and significant in all statistical models (Table 3). Consciousness level and low urine output (anuria) were dropped in the statistical models due to the perfect prediction of outcome, not statistical significance. Therefore, both variables were forced into the proposed EWS chart adopting the AVPU (alert, responds to voice or pain and unresponsive) for consciousness level from the MEOWS chart recommended in the 2003-2005 CEMACH report (Supplementary file: Appendices 1 and 2). Defining trigger as a single markedly abnormal observation (red trigger) or the combination of two simultaneously mildly abnormal observations (two yellow triggers), the corresponding values from the CEMACH MEOWS chart (Supplementary file: Appendix 1) were converted into scores of 0 (normal observation), 1 (yellow trigger) and 2 (red trigger) in the proposed chart (Supplementary file: Appendix 2). Mode of birth was scored as 0 and 1 for vaginal and caesarean births, respectively.

Discussion

This study, to our knowledge, reports for the first time, the development and validation of an obstetric diagnostic prediction model for a general obstetric population in a low resource setting using recommended methodology[10]. The final model comprised abnormal systolic blood pressure (SBP>140mm Hg or <90mmHg), high diastolic blood pressure (>90mmHg), respiratory rate (RR>40/min), temperature (>38oC), pulse rate (PR>120/min), caesarean birth, and the number of previous caesarean births. The model was 86% (95% CI 81-90) sensitive and 92% (95% CI 89-94) specific in predicting SMO with area under ROC (AUC) of 0·92 (95% CI 0·90 – 0·95). We developed an obstetric EWS with seven clinical parameters (RR, temperature, SBP, pulse rate, consciousness level, urine output and delivery mode) that performed well in predicting SMO in a low-resource setting.

A previous study in the United Kingdom [18] using a similar methodology produced an obstetric EWS with similar discriminatory properties (ROC (AUC) 0.957 (95% CI 0.923-0.991). Although that study by Carle et al. (2013) had a larger sample size (model development n = 2240) and validation n = 2200), the dataset used was for women admitted to ICU and the EWS included the fraction of inspired oxygen and arterial blood gas, these may limit its use in a low resource setting [25–27] [28]. We did not have the fraction of inspired oxygen in our dataset but we found that low SPO2 was not a significant predictor of SMO risk in our final model. It will have been useful to assess the performance of the Carle et al. (2013) EWS on our dataset but this was not possible because the clinical variables in the SMO cases of our dataset were collected as categorical (binary) variables.

We found that temperature >38^{o} C was a predictor of SMO, this was similar to the finding by Ryan et al. (2015)[29] by Singh et al. (2012)[15]. Our finding of high systolic BP as a predictor of SMO was consistent with the findings of two inpatient obstetric ward-based validation studies which used the morbidity[15,] and ICU admission as outcomes[28], and an EWS external validation study that had death as outcome [19]. However, these findings differed from the development and validation study by Carle and colleagues (2013), that used data within 24 hours of admission into the intensive care unit while the other studies used data from inpatients that had no obvious need for critical care [18].

Our report of a significant association between SMO and tachypnoea, high pulse rate, diastolic blood pressure, and low consciousness level was consistent with the findings from the ICU-based external validation study by Paternina-Caicedo and colleagues[19].

We found a significantly increased risk of SMO among women who had caesarean compared to vaginal birth, and the variable remained an important predictor of SMO in all our models during development. This informed our inclusion of the mode of birth in the proposed EWS tool (Supplementary file: Appendix 2).

Our model has an excellent predictive ability to discriminate women who developed severe maternal outcome from those who did not (AUCs consistently above 90%). The model attained similar diagnostic predictive accuracy as one developed, internally[18] and externally[19] validated using data from obstetric intensive care unit patients in the USA. Our model also performed similarly to non-obstetric cardiovascular, adult critical care and neonatal critical care score system developed. [29–31] Compared to other routinely used EWS in obstetric ward settings, our model has significantly better screening characteristics (PPV 94% CI 93-95), compared to an average of 41% was reported for 16 different EWS versions. [7] This is of particular significance, since an early warning system that generates many false positive findings may worsen clinical care, constitute a nuisance alarm by creating an excessive burden on the health system[32,33]. Potentially, the proposed chart presents an opportunity to institute life-saving interventions to improve clinical outcome. However, current evidence suggests that the use of EWS by itself is not enough to improve health outcomes and that for this tool to perform optimally, an EWS must be integrated with an outreach support system, such as a rapid response team [7,34].

Of the seven parameters in the proposed EWS chart from our analysis (Supplementary file: Appendix 2), five (temperature, pulse rate, systolic blood pressure, respiratory rate and consciousness level) were included in the majority (>80%) of the EWS published to date[7]. Delays in triage (identification of who is, or may become, severely ill and should be provided with a higher level of care) are believed to contribute immensely to an increased burden of adverse obstetric outcomes in this settings[5]. This is further confounded by the unavailability of patient monitoring devices and other diagnostic equipment,

especially in the primary healthcare settings [28]. Therefore, in addition to the inpatient obstetric wards, we believe the proposed monitoring chart can present a potentially useful triaging tool to aid timely referral in primary healthcare centres in LMICs. However, a prospective external validation study is recommended to assess the effectiveness of the EWS developed in both primary, secondary/tertiary care in other low resource settings to further substantiate these recommendations.

The main strength of our analysis lies in the robust maternal death and near-miss case data set which was prospectively collected primarily for research purpose with very few missing data (2·7% of participants), the strict adherence to diagnostic predictive model development process and reporting as recommended by TRIPOD.[10] A limitation of EWS validation studies that were addressed in our analysis is a lack of standardisation of outcome measures; this is especially common with studies using morbidity as an outcome measure, as often, this was defined based on consensus rather than standardised definitions[7]. There are several limitations to this study. Firstly, the data of SMO cases consisted of already categorised clinical variables. Although cut-offs were based on recommendations for defining specific disease conditions (such as high blood pressure) by of policy-making organisations like the WHO, it was not possible to validate different trigger thresholds for the model parameters. Secondly, lack of continuous data also made it impossible to externally validate other EWS versions like the CEMACH MEOWS and the ICU based chart developed by Carle et al. (2013)[18]. Additionally, pulse oximetry was poorly recorded in our study data set, especially in the controls where the parameter was assumed to be above 90%. Although the absence of oxygen saturation could make our proposed chart more feasible to use in low resource settings, evidence from other analyses has shown that it is a valuable predictor of death and serious obstetric complications[35–38]. It is therefore probable that this clinical variable would still contribute to a statistically developed and validated EWS decision tool in our study population. This can be investigated in an appropriately designed study in the future.

Conclusion

To the best of our knowledge, this study provides for the first time, an internally validated statistically developed diagnostic predictive model for all women admitted to obstetric wards in a low resource setting. This model was used to develop a simple score-based EWS chart that has easy to measure parameters with readily available patient monitoring tools, hence constituting a potentially useful triaging tool in low resource healthcare settings. Further work is however needed to validate this proposed chart externally in the obstetric wards as well as primary healthcare settings.

Conflict of interest

All authors have no conflict of interest.

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