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Evaluation of a novel device in the management of high blood pressure and shock in pregnancy in low-resource settings

Submission date
24/11/2015

Recruitment status
No longer recruiting

Registration date
02/02/2016

Overall study status
Completed

Last Edited
10/03/2023

Condition category
Pregnancy and Childbirth

[X] Prospectively registered

[_] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims

Every day about 800 women die in pregnancy or childbirth, and 99% of all of these deaths occur in the developing world. Women in rural communities with limited access to healthcare are at the greatest risk. The leading causes of death in these women include severe bleeding, overwhelming infections, and blood pressure problems. Many women die in pregnancy because the problem is recognised too late. In all of these instances, simply monitoring women's blood pressure and pulse could be life-saving. A woman would be recognised as being unwell and appropriately treated before serious, irreversible complications set in. In the developing world many healthcare providers do not have access to working blood pressure devices. Many devices that are available are often inaccurate in pregnancy, particularly in women with blood pressure problems. This means that unwell women go unrecognised and treatment is either delayed or not given, which can result in serious illness and even death. We have developed a simple, accurate, handheld device to measure blood pressure and pulse. This device has some special features that make it ideal for use in the developing world. It does not require medical training and anyone can use the device with minimal skill. This makes it ideal for use in communities, particularly rural settings, where untrained health workers commonly visit women and their babies. Another special feature is the 'traffic light' system; the device tells the user if the blood pressure and pulse measurements are normal (green), worrying (amber) or severely abnormal (red). This enables the device to signpost women who are unwell, or becoming unwell, to untrained observers. This will enable more appropriate and early referral to higher-level care. The device has been tested extensively and has been shown to be accurate in pregnant women, even those with blood pressure problems. The device can be charged through a regular mobile phone charger, has a long power life and a large easy-to-read screen. The device is cheap at less than £12. Through our previous work in rural community settings in Africa, we know that there is a need for access to blood pressure devices, as many clinics have no access to working, accurate machines. This study will improve access for women to have accurate measurements of their blood pressure and pulse (a fundamental part of care for women in pregnancy). Our study intends to put these simple devices into communities with the aim of improving detection of

pulse and blood pressure problems. By highlighting those who are unwell, we hope use of the device will lead to more women receiving the best, most appropriate care and fewer women dying or becoming seriously unwell from these devastating diseases.

Who can participate?
Women who are pregnant or gave birth within the last 6 weeks, and living in the study catchment areas within the study time frame.

What does the study involve?
Pregnant women should have their blood pressure checked as part of routine antenatal care. This study involves replacing the current methods to measure blood pressure with the CRADLE VSA device, which is incorporated into routine care. There are no other changes to the patient's care as part of the study. Healthcare practitioners may be asked to complete multiple-choice questionnaires or complete a log of their use of their device to assess the training materials. A sample of healthcare practitioners are also interviewed. A focus group discussion is undertaken at each site at three months.

What are the possible benefits and risks of participating?
By participating in this study, healthcare practitioners will get the chance to gain experience in using the blood pressure device and have improved access to accurate reliable equipment. Feedback provided by healthcare practitioners will help to improve the training and plan a larger study of this device in vulnerable women in pregnancy. The Microlife CRADLE VSA is used worldwide in pregnancy as a standard automated blood pressure device. We do not anticipate any risks to those using the devices or the participating women. A potential risk is that triggering of the traffic light early warning system may lead to more women being referred to a higher-level facility, thereby overwhelming the facility. Alternatively, the early warning system may give a false sense of stability of women, resulting in delay in referral. It is for this reason that the CRADLE package of care will include education about appropriate transport to facility, as well as instructions about how to manage women who do not trigger the early warning system but who are otherwise unwell.

Where is the study run from?
Morgenster Mission Hospital (Zimbabwe), Lusaka University Teaching Hospital (Zambia), Mulago Hospital, (Uganda), Haiti Hospital (Haiti), Tikur Anbessa University Hospital (Ethiopia), Zomba Hospital (Malawi), Ndola Central Hospital (Zambia), Princess Christian Maternity Hospital (Sierra Leone), Jawaharlal Nehru Medical College (India), Gimbie Adventist Hospital (Ethiopia), Mbale Regional Referral Hospital (Uganda), University of Zimbabwe (Zimbabwe).

When is the study starting and how long is it expected to run for?
October 2015 to March 2018

Who is funding the study?
Medical Research Council (UK), Department Of Biotechnology (India), Department for International Development (UK).

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
N/A

ClinicalTrials.gov (NCT)
N/A

Protocol serial number
MR/N006240/1

Study information

Scientific Title
Evaluation of the CRADLE vital sign alert device in the management of hypertension and shock in pregnancy in low-resource settings to reduce maternal mortality and morbidity: a stepped wedge randomised controlled trial

Acronym
CRADLE 3

Study objectives
Implementation of a novel semi-automated vital-sign alert device and simple education package used by healthcare providers (HCPs) at community and facility levels will reduce maternal mortality and major morbidity from the three leading causes of maternal death worldwide (obstetric haemorrhage, sepsis and pre-eclampsia) in low-income country (LIC) populations.

Ethics approval required
Old ethics approval format

Ethics approval(s)

1. Biomedical Sciences, Dentistry, Medicine and Natural & Mathematical Sciences Research Ethics Subcommittee, 26/08/2015, ref: LRS-14/15-1484
2. Individual ethics approvals have been sought and finalised from each of our international partners

Study design
Two-phased multicentre stepped wedge cluster randomised controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Maternal mortality and major morbidity from the three leading causes of maternal death worldwide: obstetric haemorrhage, sepsis and pre-eclampsia

Interventions
This is a two-phased multicentre stepped wedge cluster randomised controlled trial of the introduction of the CRADLE package (Vital Signs device and training package) to maternity care settings in eight low income countries.

Due to the stepped wedge trial design, each randomisation cluster crosses over from control to the CRADLE intervention at two-monthly intervals over the 21 month trial period. For the first two-month interval no cluster has the intervention and by 21 month all clusters will have the intervention. The intervention effect is determined by comparing data points in the intervention section of the wedge with those in the control section. This design has been selected to evaluate the intervention in a pragmatic fashion. Individual randomisation would be logistically difficult and would not measure impact and transferability at a population level. The stepped wedge design is useful where phased implementation is preferable because of logistical and practical constraints. Our LIC collaborators have indicated that this is their preferred means of participation, as a phased introduction of the intervention is more reflective of current implementation programs.

The intervention consists of the CRADLE VSA device, a device that measures blood pressure and heart rate and calculates shock index, and a simple education package that describes how to use the device. The simple education package consists of two specific short animated films on the use of the device and management of hypertension and shock and posters and alert cards. The CRADLE VSA will be incorporated into routine antenatal care as all women should have blood pressure measured regularly in the antenatal period. Therefore there is no specified treatment duration or follow up.

Intervention Type
Device

Primary outcome(s)
Primary outcome measures as of 01/04/2016 (Added 09/12/2016):
The primary outcome is the rate of a composite of maternal mortality or major morbidity (one of maternal death, eclampsia or emergency hysterectomy with no double counting) per 10,000 deliveries. We will report the effect of the intervention on the primary endpoint, on each of the

three components, and on the secondary endpoints specified. Results will be reported firstly as odds ratios, with risk ratios as a secondary comparison if the appropriate models converge. The components of the primary outcome are defined as:
1. Maternal death is defined as death during pregnancy or within 42 days of delivery (or last contact day if contact not maintained to 42 days).
2. Eclampsia is defined as occurrence of generalised convulsions or coma with increased BP during pregnancy, labour or within 42 days of delivery in the absence of epilepsy or another condition predisposing to convulsions
3. Emergency Hysterectomy is defined as surgical removal of all or part of the uterus

Primary outcome measures as of 29/02/2016:
1. Maternal death, defined as death during pregnancy or within 42 days of delivery (or last contact day if contact not maintained to 42 days)
2. Eclampsia, defined as occurrence of generalised convulsions or coma with increased blood pressure during pregnancy, labour or within 42 days of delivery in the absence of epilepsy or another condition predisposing to convulsions
3. Emergency Hysterectomy, defined as surgical removal of all or part of the uterus

Following the completion of the three month pilot phase from November 2015 to February 2016 there have been minor prospective amendments to the protocol prior to the start of the main trial in March 2016. Given the variable access to intensive care beds and low prevalence of stroke observed across our trial sites in the pilot these outcomes will not be included in the primary composite outcome. They will continue to be measured as secondary outcomes. The event rate of our existing composite primary outcome components (Maternal death, eclampsia, emergency hysterectomy) remain sufficient to maintain planned statistical power.

Original primary outcome measures:
1. Maternal death, defined as death during pregnancy or within 42 days of delivery (or last contact day if contact not maintained to 42 days)
2. Intensive Care Unit admission, defined as any admission to intensive care unit or an equivalent highest-level care environment within the trial area (or referral to the highest level care facility outside of the area) in areas where Intensive Care Unit does not exist
3. Eclampsia, defined as occurrence of generalised convulsions or coma with increased blood pressure during pregnancy, labour or within 42 days of delivery in the absence of epilepsy or another condition predisposing to convulsions
4. Stroke, defined as hemiparesis and/or blindness developed during pregnancy or in the 42 days postpartum lasting greater than 48 hours
5. Hysterectomy, defined as surgical removal of all or part of the uterus

All primary and secondary outcomes are measured consistently across the site area throughout trial duration so that the overall impact of intervention can be determined over the 21 month trial period. Interim analysis is not feasible due to the stepped wedge design.

Key secondary outcome(s))

Secondary outcome measures as of 29/02/2016:
Maternal Secondary outcome measures:
1. Intensive Care Unit admission, defined as any admission to a specific intensive care unit or an equivalent highest-level care environment within the trial area (or referral to the highest level care facility outside of the area) in areas where Intensive Care Unit does not exist
2. Stroke, defined as hemiparesis and/or blindness developed during pregnancy or in the 42 days postpartum lasting greater than 48 hours
3. Cause of intensive care admission

4. Cause of maternal death
5. Cause of emergency hysterectomy
5. Place of eclamptic fit
6. Place of maternal death

These additional secondary outcome measures have been added following the pilot experience in an effort to determine the potential benefit of the device on these outcomes.

Neonatal Secondary outcome measures
We recognise that the CRADLE intervention may reduce neonatal mortality and morbidity, but have not been chosen to evaluate these as primary outcomes, as the intervention is designed specifically to identify maternal health complications. Many of these occur postpartum and will not directly influence perinatal outcomes. Acquisition of detailed perinatal data within LIC settings would be a substantial additional cost. However, we will collect secondary outcomes including:
1. Number of stillbirths
2. Number of neonatal deaths

Original secondary outcome measures:
We recognise that the CRADLE intervention may reduce neonatal mortality and morbidity, but have not been chosen to evaluate these as primary outcomes, as the intervention is designed specifically to identify maternal health complications. Many of these occur postpartum and will not directly influence perinatal outcomes. Acquisition of detailed perinatal data within LIC settings would be a substantial additional cost. However, we will collect secondary outcomes including:
1. Number of stillbirths
2. Number of neonatal deaths

All primary and secondary outcomes are measured consistently across the site area throughout trial duration so that the overall impact of intervention can be determined over the 21 month trial period. Interim analysis is not feasible due to the stepped wedge design.

Completion date
01/03/2018

Eligibility

Key inclusion criteria
1. All pregnant/postpartum women living in Trial Area catchment areas* within the trial time frame
2. Women identified as pregnant or within the 6 weeks post-partum period, presenting for antenatal, intrapartum or postpartum care

*Catchment areas will be defined by local investigators, and include all possible outreach facilities that result in women being assessed and referred to a defined central facility/ies, prior to randomisation and remain constant throughout the study period.

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Mixed

Sex
Female

Total final enrolment
10

Key exclusion criteria
There will be no exclusion criteria, including age of women, as, from an ethical and logistical standpoint, all pregnant women (including those below the age of 16 years) should have access to blood pressure measurement during pregnancy. Data are to be collected at a cluster level rather than at an individual level.

Date of first enrolment
01/03/2016

Date of final enrolment
01/12/2017

Locations

Countries of recruitment
Ethiopia

Haiti

India

Malawi

Sierra Leone

Uganda

Zambia

Zimbabwe

Study participating centre
Morgenster Mission Hospital and Masvingo District
Reformed Church in Zimbabwe
Masvingo
Zimbabwe
PO Box 670

Study participating centre
Lusaka University Teaching Hospital
University Teaching Hospital
Lusaka
Zambia
Private Bag RW1X

Study participating centre
Mulago Hospital
Obstetrics and Gynaecology
Mulago
Uganda
PO Box 7051

Study participating centre
Haiti Hospital
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Study participating centre
Tikur Anbessa University Hospital
Woman's Health
Addis Ababa
Ethiopia
5657

Study participating centre
Zomba Hospital
Women's Health
Zomba
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Study participating centre
Ndola Central Hospital
Women's Health
Ndola

Zambia
Private Bag 1

Study participating centre
Princess Christian Maternity Hospital
Fourah Bay Road
Free Town
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Study participating centre
Jawaharlal Nehru Medical College
Women's & Children's Health Research Unit
Belgaum
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BELAGAVI-590010

Study participating centre
Gimbie Adventist Hospital
Gimbie
Ethiopia
PO Box 228

Study participating centre
Jawaharlal Nehru Medical College
Obstetrics and Gynaecology
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Study participating centre
Mbale Regional Referral Hospital
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Uganda
PO Box 921

Study participating centre

University of Zimbabwe
Obstetrics and Gynaecology
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Sponsor information

Organisation
Kings College London (UK)

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Department Of Biotechnology (India)

Funder Name
Department for International Development (UK) Global Research Programme

Alternative Name(s)
Department for International Development, UK, DFID

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2019		Yes	No
Results article	results	18/04/2019	27/08/2019	Yes	No
Abstract results	P24	17/12/2020	10/03/2023	No	No
Other publications	secondary analysis	29/03/2019		Yes	No
Other publications	secondary analysis	21/04/2021	23/04/2021	Yes	No
Other publications	Development and evaluation of a novel Vital Signs Alert device for use in pregnancy in low-resource settings	28/09/2018	10/03/2023	Yes	No
Other publications	Feasibility study results	27/04/2018	10/03/2023	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes