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A study to improve the outcomes of mothers and babies through safe and appropriate caesarean sections

Submission date
07/11/2023

Recruitment status
Recruiting

Registration date
05/02/2024

Overall study status
Ongoing

Last Edited
10/03/2026

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Caesarean section is considered a life-saving procedure for pregnant women and their babies. Yet, in low- and middle-income countries, mothers who give birth by caesarean section are 100 times more likely to die than those having the procedure in high-income countries. In these settings, caesarean sections also contribute to life-long health problems that affect the women's quality of life and their ability to safely have more children. Their babies are also at high risk of dying during or soon after caesarean section.
The three main reasons for poor outcomes after caesarean section in low- and middle-income countries are:
1. Inappropriate caesarean sections (e.g. performed 'too many, too soon' or 'too little, too late')
2. Unsafe practices in performing the procedure
3. Substandard care in labour (e.g. not culminating in vaginal birth which leads to complicated caesarean sections in advanced labour).
Many issues contribute to the above problems such as lack of knowledge and skills to undertake safe caesarean section (and to achieve safe vaginal births - both normal and by using instruments). In addition, attitudes towards caesarean section and the use of vacuum or forceps, marginalisation of midwives, dysfunctional teamwork, a culture of blame and medico-legal concerns, influence of family members and communities in decision-making, poor communication skills between women and healthcare providers and amongst clinicians, and inability to determine why caesarean sections are performed worsen the problem.
There is no single solution to these complex problems. We need to both improve the safety of caesarean sections and ensure they are only done when needed. To do this, we will co-develop evidence-based interventions that are acceptable, equitable, sustainable and which can be adapted or scaled up cost-effectively across settings, by collaborating with women and their support networks, healthcare providers, policymakers and other relevant stakeholders.

Who can participate?
The C-safe intervention is given at the health system level and includes all healthcare workers

who provide care around the time of birth. We will be inviting women and healthcare workers to take part in surveys and interviews to understand people's thoughts and feelings on the C-Safe intervention.

What does the study involve?
The C-Safe intervention is made up of three elements:
1. C-Why; promoting appropriate caesarean section (CS) through accurate reporting of CS reasons
2. C-Op; promoting safe caesarean section through safe surgery
3. C-Non; promoting safe vaginal births, including assisted births such as vacuum
The intervention will be delivered through different types of training and learning (including feeding back the outcomes of clinical cases) and will be supported by local healthcare and community champions. The intervention will be adapted to train providers in order to reduce unnecessary caesarean sections and improve the safety of the surgery. On-site support will be provided with remote support and refresher training continuing throughout the intervention.
The study will assess the impact of the C-Safe intervention through measuring and changes in the healthcare workers' practice such as caesarean section rate and assisted vaginal birth rate. It will also measure how well the intervention has been implemented and clinical outcomes such as the deaths of mothers and babies, and the need for higher levels of care such as neonatal care and intensive care.
The hospitals included will be chosen by a “cluster randomisation”; where providers working in the hospital will take part in the intervention training. All hospitals will receive the training at some point during the study, but at different time points so we can understand the impact of the training.

What are the possible benefits and risks?
There are no direct risks involved in taking part in this study and participants can choose whether or not they to take part in the training, the interviews or the surveys.
For healthcare providers; it is expected that the training will improve the ability to provide care for women giving birth and work to improve the care of women at the facilities involved. Therefore, participation could improve job satisfaction. Surveys and interviews will be arranged at a convenient time and location.
The researchers will try to organise interviews and surveys at a time and locale suitable and most confident for the women. Women will be reassured that they will not be punished or turned away from any services at the hospital if they decide not to take part.

Where is the study run from?
The study will run in India (Andhra Pradesh) and Tanzania (Mbeya)

When is it starting and how long is it expected?
The C-Safe programme commenced in September 2022; the pilot study is anticipated the start in January 2024 in India. The cluster trial is anticipated to start 12 months after this and run for 12 months.

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Prof. Shakila Thangaratinam (CI), S.Thangaratinam@liverpool.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

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Additional identifiers

Protocol serial number
MR/V035282/1

Study information

Scientific Title
Optimising maternal and perinatal outcomes through safe and appropriate caesarean sections (C-Safe) in low- and middle-income countries: a hybrid effectiveness-implementation design stepped-wedge cluster randomised trial with mixed-methods evaluation

Acronym
C-Safe

Study objectives
The C-Safe intervention will improve maternal and perinatal outcomes following caesarean section (CS), and optimise their use, through a whole systems approach targeting the entire intrapartum period. The C-Safe intervention will be co-developed with stakeholders and incorporate evidence-based intervention(s) promoting (i) timely CS when vaginal birth is not appropriate, (ii) safety of CS when performed, and (iii) respectful and safe vaginal birth, including assisted vaginal delivery (AVD), when CS is not indicated. The intervention will be underpinned by an implementation plan addressing the clinical, social, economic, cultural and policy issues around maternity care, and be acceptable, equitable, scalable and feasible.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 29/10/2023, Fernandez Foundation Institutional Ethics Committee (4-1-1230, Bogulkunta, Off Abid Road, Hyderabad – 500001, Telangana, Hyderabad, -, India; +91 (0)40 40222300; irb@fernandez.foundation), ref: 47_2023

Primary study design
Interventional

Study design
A hybrid effectiveness-implementation design stepped-wedge cluster randomized trial with mixed-methods evaluation using six methodological components:
1. Stakeholder consensus meetings
2. Baseline assessment of organisational readiness to change
3. Staff and service user surveys
4. Non-participant observations (meetings and clinical practice)
5. Qualitative research (interviews and focus group discussions)
6. Policy document review

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Labour and birth including caesarean section and assisted vaginal birth

Interventions
After a 2-month baseline period, clusters (public hospitals) will be randomised to the order in which they will receive the C-Safe interventional package for the remainder of the 12-month period, allowing 2 months for full implementation and embedding of the interventional package. The health facilities not receiving the interventional package will continue to follow usual care as per the baseline period until they receive the interventional package. Randomisation will be conducted by an independent statistician, with the order concealed from study investigators until one month before the start of the transition date. Clusters will be randomised to one of four sequences which will dictate the order of the roll-out of the intervention to clusters, stratified by country. The health facilities will be sufficiently geographically distanced to avoid issues around intervention contamination (e.g. staff moving from an intervention site to a control site and taking the intervention techniques with them).

Follow–up will be for one month after month 12 of the intervention phase.

The C-Safe intervention will include the following packages and training around the delivery of these. Audit and feedback will form part of the intervention.

The components may include but are not limited to:
1. C-Why package (decision-making tools for appropriate caesarean section, audit and feedback of caesarean section indications based on the co-developed C-Why classification system).
2. C-Op package (surgical safety interventions including the WHO surgical safety checklist, team huddle and C-Op checklist, vaginal cleansing, single dose prophylactic antibiotics, incision type, surgical drapes and colour-coded suction bottles to detect post-partum haemorrhage, uterotonics, changing gloves and instruments before wound closure, delayed cord clamping and resuscitation for the baby, clinical care handover report).
3. C-Non package (promoting vaginal birth through components of the WHO labour care guide; Supportive care, shared decision making, companionship, positioning, hydration/nutrition) and

assisted vaginal birth (decision-making tools and assisted vaginal birth training and equipment). Both parts of C-Non included delayed cord clamping and resuscitation for the baby and the C-Non checklist.

The intervention will be delivered through different types of training and learning (including feeding back the outcomes of clinical cases) and will be supported by local healthcare and community champions. The intervention will be adapted to train providers in order to reduce unnecessary caesarean sections and improve the safety of the surgery. On-site support will be provided with remote support and refresher training continuing throughout the intervention.

The study will assess the impact of the C-Safe intervention through measuring and changes in the healthcare worker's practice such as caesarean section rate and assisted vaginal birth rate. It will also measure how well the intervention has been implemented and clinical outcomes such as the deaths of mothers and babies, and the need for higher levels of care such as neonatal care and intensive care.

The hospitals included will be chosen by a “cluster randomisation”; where providers working in the hospital will take part in the intervention training. All hospitals will receive the training at some point during the study, but at different time points so the researchers can understand the impact of the training.

Intervention Type
Behavioural

Primary outcome(s)
Current primary outcome measures as of 24/06/2025:
The main outcomes are those measuring the change in practice and are likely to lead to improvements in clinical practice.
Co-Primary outcomes are:
1. Caesarean section rate measured as the number of caesarean section births out of the number of total births in Robson groups (1-4), which are defined as:
Group 1: Number of nulliparous women, with a singleton fetus with a cephalic presentation at term gestation (≥37+0 weeks) in spontaneous labour
Group 2: Nulliparous, singleton, cephalic, term births with induced labour or prelabour caesarean section
Group 3: Multiparous, singleton, cephalic, term births without previous caesarean section in spontaneous labour
Group 4: Multiparous, singleton, cephalic, term births without previous caesarean section with induced labour or prelabour caesarean section
2. Adherence to safe perioperative measures during caesarean section which is defined as adherence to 4 out of 5 C-Op components (prospective us of the WHO CS modified Surgical Safety checklist, administration of prophylactic antibiotics 30-60 minutes before skin incision, vaginal cleansing before procedure, administration of prophylactic uterotonics immediately after birth of baby, and changing of gloves and instruments prior to sheath closure).

Previous primary outcome measures:
The main outcomes are those measuring the change in practice, and likely to lead to improvements in clinical practice. Changes in more than one process outcome will be required to improve maternal and perinatal clinical outcomes, therefore the main outcomes include the following:
1. Caesarean section rate measured as the number of caesarean section births out of the

number of total births taking place per month
2. Assisted vaginal birth rate measured as the number of assisted vaginal births out of the number of total births taking place per month
3. Spontaneous vaginal birth rate (not including assisted vaginal births) measured as the number of (unassisted) vaginal births out of the number of total births taking place per month
4. Rates of the mode of birth in Robson groups (1-4) measured as 1. The Caesarean section rate in each of the Robson groups is listed below; 2. The Assisted vaginal birth rate in each of the Robson groups listed below; and, 3. The Spontaneous vaginal birth rate in each of the Robsons groups listed below
Robson groups are defined as:
Group 1: Number of women who are nulliparous, with a singleton fetus with a cephalic presentation at term gestation (≥37+0 weeks) in spontaneous labour;
Group 2: Nulliparous, singleton, cephalic, term births with induced labour or prelabour caesarean section;
Group 3: Multiparous, singleton, cephalic, term births without previous caesarean section in spontaneous labour;
Group 4: Multiparous, singleton, cephalic, term births without previous caesarean section with induced labour or prelabour caesarean section;
5. Indications for caesarean sections measured using main and associated indications recorded according to the C-Why classification system using the C-Why audit tool looking at a percentage of total CS per month.
6. Use of C-Safe checklists measured as partial or total completion of C-Op checklists per month out of all CS birth and C-Non (AVB) checklists per month out of all assisted vaginal births
7. Delivery of the C-Safe packages measured as partial or total administration of the C-Op package components out of all CS birth and C-Non package components out of all assisted vaginal births.

Key secondary outcome(s)

Current secondary outcome measures as of 24/06/2025:
Implementation, acceptability, equity and maternal and perinatal mortality and morbidity (clinical outcomes).

Implementation outcomes include the following:
1. Reach (measured as the proportion of women who receive the C-Safe intervention at 3 months after implementation)
2. Adoption (measured as the proportion of healthcare professionals trained at 3 months after implementation)
3. Fidelity (measured as the proportion of individual intervention components given as specified at 3 months after implementation)
4. Adaption (measured as the number of intervention components modified at 3 months after implementation)
5. Appropriateness (measured as perceived fit of the intervention at 3 months after implementation)

Acceptability and equity outcomes include the following:
1. Acceptability to women and healthcare providers measured using interviews, surveys and observations at baseline, end of month 6 and month 12
2. Barriers to intervention delivery or study conduct measured using interviews, surveys and observations at baseline, end of month 6 and month 12
3. Patient-reported outcomes such as dignity, information sharing, and positive birth experience, measured using interviews, surveys and observations at baseline, end of month 6 and month 12

Clinical outcomes include the following and will be collected monthly throughout the trial period:
Maternal:
1. Postpartum haemorrhage (defined as blood loss ≥500 ml after birth) measured for all births
2. Surgical site infection (defined as an infection that occurs within 30 days after the operation and involves the skin and subcutaneous tissue of the incision (superficial incisional) and/or the deep soft tissue (for example, fascia, muscle) of the incision (deep incisional) and/or any part of the anatomy (for example, organs and spaces) other than the incision that was opened or manipulated during an operation (organ/space), measured until discharge from hospital.
3. Number of instrumental births (defined as the number of babies whose birth was facilitated by an instrument) as a proportion of total vaginal births and total births
4. Number of spontaneous vaginal births (defined as the number of babies birthed vaginally without assistance of an instrument) as a proportion of total births and total vaginal births
5. Major organ injury (defined as damage to bladder, bowel or ureters) during caesarean section surgery
6. Perineal tear (1st, 2rd, 3rd or 4th degree tear (defined as a tear that extends into the anal sphincter or the lining of the anus or rectum)) occurring in vaginal births
7. Oasis - defined as 3rd degree tear (extending into anal sphincter muscles) or 4th degree tear (further involving the lining of rectum or anus) occurrence in vaginal births.
8. Episiotomy (defined as a cut made at the opening of the vagina during birth to aid a difficult delivery) measure in all vaginal births
9. Length of hospital stay (defined as length of time a woman was in hospital following birth (vaginal or CS)), calculated in days and hours
10. Maternal death (death of a mother from any cause during and after CS up until discharge) as a proportion of women having CS
11. Return to theatre (defined as mother returning to theatre for further surgical procedure following CS), recording until discharge, or on admission within 30 days
12. Hysterectomy (required for any cause during or after CS until discharge) as a proportion of women having CS.
13. Admission to ITU (defined as a woman requiring admission to ITU for higher-level care after CS) was recorded until discharge in all women having CS.

Neonatal composite components:
1. Total number of stillbirths (defined as the death of a baby after 28 weeks of gestation (defined by WHO), but before or during birth. Includes total numbers of fresh and macerated stillbirths in babies born vaginally and by CS.
2. Neonatal death (defined as the death of a baby who is born alive but dies during the first 28 days of life), measured until discharge from the hospital.
3. Admission to the neonatal unit for more than 24 hours of treatment (defined as the admission of a baby to receive additional neonatal care or observation), measured until discharge from the hospital

Uptake of C-Non components (in all vaginal births), including:
1. Reviewed birth preference (was there a discussion around women's birthing choices and available options)
2. Presence of a birth companion (is the woman offered or allowed the option of having a person of her choosing present during labour, where possible and desired)
3. Information about birth analgesia provided (was there a discussion about available pain relief options (both pharmacological and non-pharmacological))
4. Mobilisation in labour (was the woman encouraged to mobilise and change position to aid labour progress; what positions were tried?)
5. Hydration and nutrition (was the woman offered food and drink throughout labour)

6. Initiation of breastfeeding (was breastfeeding initiated within one hour after birth); also measured in CS births.
7. Delayed cord clamping (defined as a practice where the umbilical cord is not clamped and cut immediately after birth, but delayed a minimum of 30 seconds); also measured in CS births.
8. Skin-to-skin (defined as a baby being put onto their mother's skin immediately, or very shortly, after birth); also measured in CS births.

Previous secondary outcome measures:
Implementation, acceptability, equity and maternal and perinatal mortality and morbidity (clinical outcomes).

Implementation outcomes include the following:
1. Reach (measured as the proportion of women who receive the C-Safe intervention at 3 months after implementation)
2. Adoption (measured as the proportion of healthcare professionals trained at 3 months after implementation)
3. Fidelity (measured as the proportion of individual intervention components given as specified at 3 months after implementation)
4. Adaption (measured as number of intervention components modified at 3 months after implementation)
5. Dose (measured as proportion of individual intervention components delivered at 3 months after implementation)
6. Appropriateness (measured as perceived fit of the intervention at 3 months after implementation)

Acceptability and equity outcomes include the following:
1. Acceptability to women and healthcare providers measured using interviews, surveys and observations at baseline, end of month 6 and month 12
2. Barriers to intervention delivery or study conduct measured using interviews, surveys and observations at baseline, end of month 6 and month 12
3. Patient-reported outcomes such as dignity, information sharing, and positive birth experience, measured using interviews, surveys and observations at baseline, end of month 6 and month 12

Clinical outcomes include the following and will collected monthly throughout the trial period:
Maternal:
1. Postpartum haemorrhage (defined as blood loss ≥500 ml after birth)
2. Surgical site infection (defined as an infection that occurs within 30 days after the operation and involves the skin and subcutaneous tissue of the incision (superficial incisional) and/or the deep soft tissue (for example, fascia, muscle) of the incision (deep incisional) and/or any part of the anatomy (for example, organs and spaces) other than the incision that was opened or manipulated during an operation (organ/space), measured until discharge from hospital.
3. Sepsis (defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or postpartum period) measured until discharge from hospital.
4. Death (defined as death from any cause related to or aggravated by pregnancy or its management (excluding accidental or incidental causes) during pregnancy and childbirth or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy), measured until discharge from hospital.
5. Caesarean hysterectomy (defined as the removal of the uterus at the time of caesarean section)
6. Major organ injury (defined as major organs such as bladder or bowel damaged during caesarean section surgery)
7. 3rd/4th degree tear (defined as a tear that extends into the anal sphincter or the lining of the

anus or rectum)
8. Admission to intensive care (defined as admission of an acutely unwell mother to receive critical medical care), measured until discharge from hospital

Perinatal:
1. Stillbirth (defined as the death of a baby after 28 weeks of pregnancy, but before or during birth)
2. Neonatal death (defined as the death of a baby who is born alive but dies during the first 28 days of life), measured until discharge from hospital.
3. Apgar score (defined as standardised assessment for infants after birth using five components: 1) color, 2) heart rate, 3) reflexes, 4) muscle tone, and 5) respiration, each of which receive a score of 0, 1, or 2, reported at 1 minute and 5 minutes after birth)
4. Admission to neonatal unit (defined as the admission of a baby to receive additional neonatal care or observation), measured until discharge from hospital
5. Seizures (defined as fits in the baby from birth), measured until discharge from the hospital

Completion date
31/08/2027

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 24/06/2025:
The inclusion and exclusion criteria will be the same for the field testing phase and the cluster trial phase, with the only exception being that the site used in the trial phase will not be eligible for inclusion in the cluster trial.

Cluster:
Health facilities are eligible for inclusion if:
1. Urban or peri-urban public facility
2. Secondary or tertiary-level
3. Providing comprehensive emergency obstetric care over 12 months
4. A minimum of 2,000 births/year

Participants:
Healthcare professionals:
All healthcare professionals working in a maternity setting and delivering the interventional package will be included as participants. This includes but is not limited to midwives, nurses, nurse-midwives, anaesthetists, neonatologists, obstetricians, junior doctors/ medical officers /residents/trainees and clinical officers. Healthcare administrators and managers in charge of the maternity wards or health facilities will be included as participants. This may include, but is not limited to, the head of obstetrics, matron-in-charge, or medical/clinical director.

Women:
All women and pregnant people attending facilities for birth and receiving the interventional package will be included if they are giving birth during the time their site is randomized to the C-Safe interventional package.

Previous participant inclusion criteria:
The inclusion and exclusion criteria will be the same for the field testing phase and the cluster trial phase with the only exception being the site used in the trial phase not being eligible for inclusion in the cluster trial.

Cluster:
Health facilities are eligible for inclusion if:
1. Urban or peri-urban public facility
2. Secondary or tertiary-level
3. Providing comprehensive emergency obstetric care over 12 months
4. Around 4,000 births/year

Participants:
Healthcare professionals:
All healthcare professionals working in maternity setting and delivering the interventional package will be included as participants. This includes but is not limited to midwives, nurses, nurse-midwives, anaesthetists, neonatologists, obstetricians, junior doctors/ medical officers /residents/trainees and clinical officers. Healthcare administrators and managers in charge of the maternity wards or health facilities will be included as participants. This may include but are not limited to the head of obstetrics, matron-in-charge, or medical/clinical director.

Women:
All women and pregnant people attending facilities for birth and receiving the interventional package will be included if they are giving birth during the time their site is randomized to the C-Safe interventional package.

Participant type(s)
Health professional, Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Sites used in the field-testing phase will not be eligible to participate in the stepped-wedge randomized trial
2. Sites are not providing Comprehensive Emergency Obstetric and Newborn Care
3. Sites that were or are part of another intervention trial, or if any components of the C-Safe interventional package were previously tested on them
4. Co-enrolment with sites with existing related studies will be discouraged

Date of first enrolment
28/02/2024

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
India

Tanzania

Study participating centre
District Hospital Tenali
Plots, NTR Road Amaravathi, Chenchupet
Tenali
India
522201

Study participating centre
Tukuyu District Hospital
P.O. Box 148
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Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

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

Results and Publications

Individual participant data (IPD) sharing plan
Requests for data generated during this study will be considered by the C-Safe team. Data will typically be available 6 months after the primary publication unless it is not possible to share the data (for example: the trial results are to be used as part of a regulatory submission, the release of the data is subject to the approval of a third party who withholds their consent, or University of Birmingham is not the controller of the data).

Only scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. The request will be reviewed by the University of Birmingham Data Sharing Committee in discussion with the CI and, where appropriate (or in the absence of the CI) any of the following: the trial sponsor, the relevant Programme Management Group (PMG), and independent TSC.

A formal Data Sharing Agreement (DSA) may be required between respective organisations once the release of the data is approved and before data can be released. Data will be fully de-identified (anonymised) unless the DSA covers the transfer of participant-identifiable information. Any data transfer will use a secure and encrypted method.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	26/10/2023	22/11/2023	No	Yes