Protocol

Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project

Sponsor

Wits Health Consortium

CI

GJ Hofmeyr

Synopsis

Emerging evidence suggests that uterine suction tamponade is more effdective than balloon tamponade. The currently available registered device (Jada) is unaffordable in LIMCs. We propose to conduct 'proof of concept' clinical testing of a purpose-designed, affordable device among 40 consented participants at risk of postpartum haemorrhage following vaginal or caesarean birth. Evaluation will include a randomly allocated (1:1) control group.

Context

Excessive bleeding after childbirth (postpartum haemorrhage, PPH) causes many deaths worldwide, most of which are avoidable with proper treatment. PPH usually occurs because the womb (uterus) does not contract enough after birth to compress the bleeding vessels. When medical methods fail, standard care has been to insert a balloon into the uterus and inflate it with saline. A recent development has been to replace this balloon with a suction catheter which assists uterine contraction thus stopping the bleeding. There is increasing evidence that this is more effective than a balloon, and in the USA, the FDA-approved Jada suction device has become the mainstay of treatment for persistent PPH with >90% success rates.

The current cost of the disposable Jada device (available only in the USA and Canada at US$1200 each) puts it far out of reach of the low-income settings where most PPH deaths occur, leading to global inequity in care. In this study we will test an affordable suction tube uterine tamponade device to expand access to this life-saving technology.

South African Integrated Maternal and Perinatal Care Guidelines

Suction tube uterine tamponade with off-label use of the Levin stomach tube is included in the South African Integrated Maternal and Perinatal Care Guidelines (page 116 "Intra-uterine suction with NG tube (100mmHg)" and 117: "Consider a suction tube uterine tamponade as an alternative to balloon tamponade:

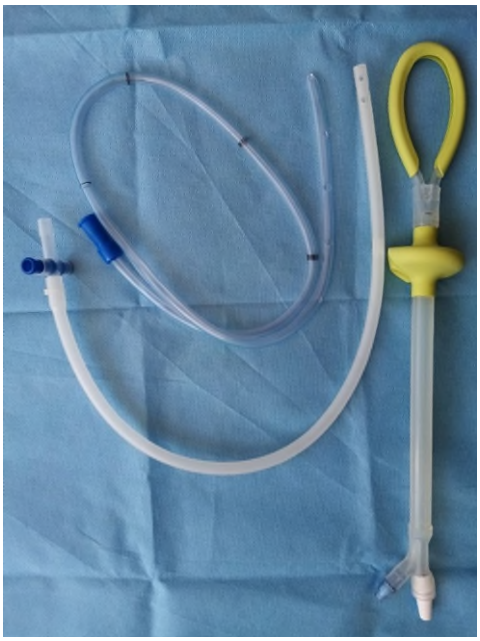
Observational comparative studies have shown that vacuum induced tamponade is 7x more effective than balloon tamponade")
https://knowledgehub.health.gov.za/system/files/elibdownloads/2024-10/Integrated%20Maternal%20and%20Perinatal%20Care%20Guideline_23_10_2024_0.pdf

The U-STAT Device

In collaboration with Sinapi Biomedical we have used our longstanding research and clinical experience with suction tube uterine tamponade using the Levin stomach tube off-label, to develop a low-cost suction device essentially similar to the well-validated Levin stomach tube but specifically designed for uterine tamponade, as well as a manual suction source to provide suction without the need for electricity.

Figure 1

1. (Top, coiled) improvised Suction Tube Uterine Tamponade (FG24 Levin stomach tube)
2. (Middle) insertion tube for the Ellavi Uterine tamponade balloon (with balloon removed) which forms the basis for the proposed purpose-designed Uterine Suction Tube Assisted Tamponade (U-STAT) device
3. (Right) Jada device (Organon)



Aims and objectives

Our overall aim is to improve access to suction tube uterine tamponade for the treatment of PPH globally.

The specific objective of the current study is to conduct 'proof of concept' clinical testing of a purpose-designed device. The device is in essence very similar to the off-label Levin stomach tube for which we have extensive research and routine clinical use evidence of safety, acceptability and clinical effectiveness.

Potential benefits and applications

- An affordable device will address current global inequity in access to this life-saving technology

- Novel features of the device will make it uniquely suitable for widespread application including during or after elective caesarean birth and use by midwives or ambulance personnel and in rural settings without access to electricity.
- Current clinical evidence suggests that a plain tube-like device may be simpler and less painful to insert than currently registered more complex technology.

Background

For refractory PPH unresponsive to medical treatment, uterine balloon tamponade (UBT) is currently recommended by WHO and by NICE in the UK. However, systematic reviews have found that the effectiveness of UBT is unclear,[1,2] and WHO has indicated the need for further research.[3] An alternative to UBT is suction tube uterine tamponade (STUT). Negative intrauterine pressure is used to contract the uterus and thus reduce bleeding.

A disposable UST device (Jada, Organon), was approved by the US Federal Drug Agency, based on an observational study in North America. The Jada device has become standard of care in many US institutions, with reassuring post-marketing data on 800 cases.[4] Large observational studies report that suction tamponade (Jada) compared with balloon tamponade (Bakri) reduce severe morbidity.[5,6]

Small, randomized trials have found better outcomes with simple suction tube tamponade than balloon tamponade, and significantly less experience of severe pain.[7,8]

Suction tamponade to arrest uterine bleeding is equally relevant to vaginal and caesarean birth (CB). Post-marketing data on 800 cases treated with the Jada device included an 84% success rate among 270 cases following CB.[4] However, use of the Jada device following CB would be restricted to cases in which the uterine cervix is sufficiently dilated to accommodate the bulky device.

Caesarean birth (CB) is increasing globally, with concomitant increase in caesarean morbidity and mortality. CB complications have been identified by WHO as a major global health problem. Blood loss at CB has been measured as mean 558mL (± 496 mL), with 5% losing >1300 mL.[9]

There are three distinct potential benefits of uterine suction tube placement at CB. Firstly, during closure of the uterine incision, the suction tube acts as an efficient ‘sump’ suction to clear blood from the surgical field, facilitating closure. Secondly, after closure of the uterine incision, the suction tube minimises blood loss by rapidly stimulating and maintaining uterine contraction and retraction. Thirdly, the presence of the STUT catheter efficiently monitors blood loss both during and after surgery, allowing prompt treatment of any PPH.

We have identified and reported on a low-cost (GBP 0.50p), widely available soft plastic catheter (the Levin FG 24 stomach tube) for STUT.[10,11]

WHO is conducting a large, randomised trial of treatments for refractory PPH in Vietnam (RED). Our preliminary data on the improvised STUT method was evaluated by the WHO ethics and scientific committees and approved for use as the only suction tamponade method in this trial (versus the Sinapi Ellavi balloon

tamponade method and the local standard of care (Foley balloon)). JH wrote the original proposal for the RED study and serves as an advisor to the study. AW is on the technical advisory group and has spoken to the clinicians in Vietnam who reported being impressed by the rapid cessation of bleeding with the STUT device. Over 500 participants have been recruited to date.

Use of an improvised suction catheter has also been reported from Switzerland.[12] Recently, a small randomised trial in India reported better results with a simple stainless steel suction catheter versus condom balloon tamponade.[7] We have conducted a multicentre randomized trial of STUT versus UBT (Bakri or Ellavi balloons) in South Africa and Colombia, similarly favouring suction tamponade.[8] Reporting severe pain during the procedures was less frequent in the STUT group ($p = 0.01$). This was to be expected, given that the suction tube is less bulky than the balloon for insertion. Thus, available evidence to date favours suction tamponade over balloon tamponade for refractory PPH.

Suction tamponade with the Jada device has become standard of care in settings with access to the technology in North America. However, the device is unaffordable in low resource settings.

Our considerable research and clinical experience indicate that a simple suction tube device is likely to be easier, quicker and less painful to insert than more complex devices, and for these reasons may in practice be more effective than the currently available complex device. A huge cost differential will ensure greater access to this lifesaving technology in both high- and low-resource settings.

In this study we progress from the current improvised off-label use of a stomach tube, to use of a suction tube device specifically designed for the purpose and provisionally known as the U-STAT (Uterine Suction Tube Assisted Tamponade) device.

This will achieve maximal efficiency and overcome regulatory and professional barriers to use of off-label devices. Because the U-STAT is geometrically very similar to the off-label Levin tube, the considerable research and clinical experience with the Levin tube is applicable to the U-STAT device.

The advantages of a simple tube suction device over a more complex system such as the Jada system are:

- Improved access globally due to the reduced cost
- Simpler and more rapid insertion of a suction tube (the U-STAT is less bulky and does not require inflation of a cuff)
- Less painful for the patient – in our randomized trial, the report of severe pain during the procedure was significantly less frequent with the suction tube than with the bulkier balloon tamponade device (Bakri or Ellavi), which are in turn less bulky than the Jada device
- More rapid initiation of suction. Apart from the more rapid insertion, our U-STAT device is supplied connected to a manual suction device to establish immediate suction on insertion. Once electronic suction is available, the device can be connected to it, or in settings without access to electronic suction such as out of hospital emergencies, during ambulance transfer, or during transfer form theatre to the ward, suction would be maintained with the manual suction device.

- Removal would also be expected to be less painful with a smooth tube than with a complex, bulkier device

	Improvised STUT suction tube	Proposed U-STAT tamponade device	Jada suction tamponade device
Ease of insertion	Easy insertion due to smooth tubular shape	Similar to STUT	More bulky and complex
Pain during insertion	Proved less than balloon devices, potentially less than Jada	Similar to STUT	More bulky and complex
Time to complete insertion	Rapid	Rapid	Delayed by inflation of cuff
Effectiveness (no head-to-head comparisons yet)	More effective than balloon tamponade (RCT's)	Similar to STUT	More effective than balloon tamponade (no RCT's)
Ease of removal	Easy removal due to smooth tubular shape	Similar to STUT	More bulky and complex
Use at or after elective caesarean birth	Suitable (proof of concept study in 45 caesarean births) (Hofmeyr IJGO 2019 doi: 10.1002/ijgo.12889)	Similar to STUT	Limited by cervical dilation sufficient to accommodate bulky device
Use in out of hospital and resource-limited settings	Limited by access to electronic suction source	Integrated manual suction attachment (optional)	Limited by access to electronic suction source
Cost	GBP 0.50p	Target GBP 10	USD 1200
Main factor limiting access	Lack of regulatory approval	Target: regulatory approval at affordable cost	Cost

Table 1. Target Product Profile comparison with alternative technologies

This application is an investigator-initiated, University-sponsored academic research program. Sinapi Biomedical are sub-contracted to supply the device. Sinapi manufactures a CE marked Ellavi balloon uterine tamponade system (Fig 1). The central tube is very similar to the Levin tube, but without the multiple suction holes, and served as the starting point for development of the U-STAT device.

Methods

This exploratory proof of concept (POC) clinical trial will build on our experience with our initial clinical studies of the improvised STUT device. This initial trial is designed to assess essential safety, performance, feasibility and acceptability and to give an indication of effectiveness and suitability for a substantive randomized effectiveness trial. It will include a limited number of participants (intervention arm n=40, control arm n=40).

Study type: Investigator-initiated, academic, non-commercial study.

Study Sponsor: Wits Health Consortium, a subsidiary of University of the Witwatersrand

Study Design: Prospective intervention study

Study Sites: Frere/Cecilia Makiwane hospitals, South Africa

Study Duration: Four months

Study Population: Women 18 years old or more with risk factor(s) for PPH, for planned vaginal or caesarean birth; no serious medical conditions.

Inclusion Criteria

- Age 18 years and older
- Planned vaginal or caesarean birth
- One or more risk factors for PPH. These include
    - Previous PPH
    - Hypertension and pre-eclampsia
    - Induction of labour
    - Emergency caesarean birth
    - Anaemia
    - Multiple pregnancy
    - Polyhdramnios
    - Macrosomia
    - Antepartum haemorrhage
- No serious medical conditions
- Provision of signed written informed consent

Intervention: Suction Tube Uterine Tamponade (STUT) using the purpose-designed soft plastic suction catheter inserted after vaginal birth or during caesarean birth. Low-pressure suction applied (approx. 100mmHg). Suction stopped after 30 minutes. If no further bleeding, tube removed. If bleeding resumes, suction continued. If bleeding not controlled within 20 min (or sooner if clinically indicated), proceed to further management according to local standard of care protocols (these might include additional uterotonics, tranexamic acid, compression methods, uterine balloon tamponade or laparotomy).

Control: This is a pilot proof of concept study with sample size insufficient for a formal randomized comparison. In order to have a valid comparator, participants will be randomly allocated to an intervention and control group (approx. 40 per group). No p values will be calculated. Comparisons will be as risk ratios or mean differences with 95% confidence intervals.

Outcomes

Baseline demography and clinical data will be recorded.

Primary: The primary outcome is the combined frequency of adverse device effects and device deficiencies up to discharge from hospital.

Adverse device effects (ADEs) encompass any adverse event with a reasonable causal relationship resulting from insufficient or inadequate instructions for use; problems with the deployment, implantation, installation, or operation of the device; malfunction of the device; or user error or intentional misuse of the device. They will include device deficiencies such as device expulsion / falling out of the uterus, failed maintenance of suction pressure and tube blockage.

A Serious Adverse Device Effect (SADE) is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. An example of this would be the need for further intervention to treat trauma caused by the device (e.g. sutures, laparotomy, etc).

Secondary efficacy outcomes will include:

1. Measured blood loss within 30 minutes after insertion (ml)
2. Blood loss >500ml
3. Blood loss >1000ml
4. Efficiency of suction (assessed through ultrasound assessment of residual blood in the uterus at 30 minutes or blood expressed from the uterus after tube removal)
5. Blood pressure, pulse and shock index 15 minutes after vaginal birth or caesarean
6. Change in routinely collected haemoglobin levels pre delivery to post delivery
7. Blood transfusion
8. ICU admission
9. Death
10. Functionality and acceptability:
    a. Active bleeding from the uterus continuing for more than 10 minutes (main efficacy outcome).
    b. Any adverse event
    c. Pain experienced (No pain/Mild /Severe/Unbearable)
    d. Need for Additional interventions to stop bleeding (e.g. more uterotonics, compressive measures, UBT, laparotomy, hysterectomy)
    e. Was STUT effectively inserted? (Yes/No/Unknown)
    f. How easy was it for health care providers to insert the Suction Tube Uterine Tamponade (easy/moderately difficult/Difficult/failed)

g. Did the suction tube remain in place in the uterus until removal (Yes/No/Unknown)
h. Did the suction tube establish a good seal (no loss of suction) (Yes/No/Unknown)
i. Did the suction tube interfere with or facilitate examination for and management of lower genital tract bleeding after vaginal birth (Facilitated/Interfered/Neither/not applicable/Unknown)
j. Did the suction tube interfere with or facilitate surgical exposure during caesarean birth (Facilitated/Interfered/Neither/Unknown)
k. Was there any blockage of the suction tube (Yes/No/Unknown)

Recruitment and consent

We plan to approach women at increased risk of PPH awaiting caesarean or induction of labour, pre-labour or in early labour and provide written and/or video information to them. They will be given time to discuss participation with friends and family and then invited to provide signed consent. Consent will be confirmed verbally immediately after birth, prior to device insertion.

Sample size

We aim to use the U-STAT in 40 participants, with a minimum of 25% being vaginal births and 25% caesarean section. 35 participants will provide 90% confidence that the true rate of adverse device effects and device deficiencies is under 10% (+/- 10%). The sample is increased to 40 to account for any unexpected procedural difficulties in the first 5 recruits.

Procedures

Participating sites will be supplied with a ‘PPH emergency trolley’ containing all the supplies needed for STUT and emergency treatment of PPH, as well as forms for screening, enrolment, randomization and data collection. After vaginal birth, the suction tube will be inserted under sterile conditions transvaginally into the uterine cavity. Suction will be applied either with the manual suction device or with a surgical suction unit, set at 100mmHg suction pressure. If there is excessive bleeding which is not controlled by the STUT, the suction tube will be removed and management continued according to local protocols. If effective, the STUT suction will be interrupted every 30 minutes, and removed as soon as bleeding is controlled without suction. All other care will follow local practice. Blood loss will be measured from enrolment until bleeding is controlled (minimum 30 minutes), using a blood collection drape or Maternawell tray, plus blood collected in the UVT suction bottle, surgical suction and swabs.

During caesarean, the suction tube tip will be placed in the fundus and the connection end passed trans-cervically to be connected to the suction by a research assistant.

For both methods, suction of approximately 100mmHg will be achieved using a standard clinical electronic suction apparatus, or the manual suction device. Participants will receive routine monitoring and care and will be followed up until discharge from hospital. Participants and providers will complete structured and open-ended questionnaires to document acceptability, ease of the procedure, discomfort, and satisfaction.

Safety

Care for all participants in the study will be optimized in the following ways:

Regular on-site training of staff in the prevention and management of PPH as well as uterine suction tamponade insertion will be conducted. Staff in the participating hospital are familiar with routinely inserting suction tube uterine tamponade, in accordance with SA national integrated perinatal and maternity care guidelines.

Rapid interventions will be facilitated by the provision of a 'PPH emergency trolley' in the labour wards, containing a supply of all consumables needed for management of PPH (IV cannulas, IV fluids, tranexamic acid, blood collection tubes and forms, light and retractors for examining the lower genital tract and UVT devices). Thus, emergency care will be able to be instituted without delay.

Quality assurance

Trial procedures have built on experience and methods developed for previous trials conducted in the Unit.

Before recruitment

CONSORT principles will be adapted for conduct and reporting of the trial. The protocol will be registered with SANCTR. The draft analysis plan will be finalised before recruitment begins.

Participating research staff will be trained to correctly describe the study to potential participants, administer the consent and screening forms, and correctly fill out paper CRFs. Guidelines will be prepared for these procedures and for entering data on the case record forms. The guidelines will list all data management activities and specify the roles and responsibilities of all personnel involved in the study. We will pilot the trial procedures, including the use of CRFs, before recruitment. Refresher courses will be conducted as considered necessary.

During recruitment

Enrolment will take place immediately after birth of the baby when the participant's name is entered in the enrolment register and allocation takes place by opening the next in a consecutively numbered series of opaque sealed envelopes with allocation cards in computer-generated random sequence in balanced blocks of variable size, stratified by mode of birth. Participants will remain in the trial whether or not the intervention is applied, on the 'intention to treat' principle. Good Clinical Practice (GCP) procedures will be followed.

A clinical checklist will be completed by the attending clinician, which will form part of the patient clinical record. Data will be entered onto paper or electronic CRFs by the research staff.

Quality control will be performed on-site: the research staff will be responsible for ensuring that the CRFs are correctly filled out. Completed CRFs will be checked against the original patient records for correct completion. Any discrepancies will be immediately addressed.

Data management

Because of the small number of participants and limited data per participant, complex data entry strategies will not be needed. Data will be entered onto paper or electronic CRF's, checked for accuracy at source, and stored in a locked filing cabinet or password-protected computer. The data will be entered onto an excel spreadsheet and analysed using Epi Info software.

Adverse events and serious adverse events, whether thought to be related to the trial intervention or not, will be recorded by the site PIs on standard adverse events forms which will be submitted to the University ethics committee and DSMC.

Data protection procedures

The following measures will be taken to ensure participant confidentiality:

- Trial data sets for each participant will be identified by a unique ID number, not the participant's name
- The trial register of names and trial ID numbers, and consent forms will be kept separate from the CRFs
- Trial documents will be kept securely under lock and key and will not be accessible, other than to the research teams
- Data will be entered by trial ID number onto a password-protected database to which only trial staff will have access
- The trial report will not contain the names of any participants
- After completion of the trial, the trial documents will be kept under lock and key for five years

Personal information

The clinical trial will include use of personal demographic and clinical information of participants. The information will be de-identified using a trial ID number and stored in a password-protected computer. Paper trial documents will be stored under lock and key.

Data analysis

Data management will be conducted by the Liverpool University Clinical Trials Unit. The locked database will then be passed to the investigators for analysis.

For continuous variables, the number of participants, number of missing values, minima, maxima, means and standard deviations will be reported, with 95% confidence intervals. If distribution is not normal, medians and interquartile range (IQR) will be reported.

For categorical variables, the number of participants, number of missing values and percentages will be reported, with 95% confidence intervals.

Comparisons will be expressed as risk ratios or mean differences with 95% confidence intervals. As the study is not powered for statistical analysis, no p values will be reported.

Data sharing and access

Data will be made available after publication of results on reasonable request based on an ethically approved research protocol. Data sharing is included in the participant information.

Trial registration

The protocol will be registered with SANCTR and ISRCTN.

Research team

GJH is a senior researcher with expertise in clinical trials. **M S-M** is a researcher with many years' experience conducting non-regulatory and regulatory clinical trials

The Trial Management Group will be responsible for governance and oversight. GJH will be overall responsible for the clinical trial conduct, whilst M S-M will supervise the clinical trial.

Facilities

Frere and Cecilia Makiwane Hospitals, East London, South Africa, provide an integrated Obstetrics and Gynaecology service with shared consultant cover. GJH is on the clinical staff and will have access to a large patient population for conducting the clinical trial (10 000 births /year). The clinical trial procedures will take place within the context of routine care in the hospitals. Suction tube uterine tamponade with off-label use of the Levin stomach tube is in routine use at the hospitals, in accordance with the South African Integrated Maternal and Perinatal Care Guidelines (page 116 and 117), and clinical staff are experienced in its use. https://knowledgehub.health.gov.za/system/files/elibdownloads/2024-10/Integrated%20Maternal%20and%20Perinatal%20Care%20Guideline_23_10_2024_0.pdf

DSMC

Because of the limited study size, a small DSMC will be appointed, primarily to adjudicate causality of any adverse events. There will be no interim analyses. The preliminary members, who have agreed to serve, are senior obstetrician researchers Prof Gerhard Theron (Chair) and Prof Lut Geerts.

Ethics and Responsible Research

The clinical trial will be conducted only after approval by the Walter Sisulu University Human ethics committee, the Eastern Cape Provincial research unit and the hospital management, and in compliance with current ethical standards for clinical research, including written informed consent, participant anonymity, protection of data and data sharing considerations. Community input will be obtained via a Community Advisory Board. Researchers will have valid 'Good Clinical Practice' in research certification.

Societal acceptance is expected to be high as patients place a high value on measures to improve safety with respect to serious complications such as postpartum haemorrhage.

The trial will be limited to a small number of generally healthy participants (40 intervention, 40 control) with an identified risk factor for postpartum haemorrhage. The Suction tube uterine tamponade procedure has been used extensively in published research both prophylactically and therapeutically as well as in routine clinical practice in our unit, with no complications identified to date.

Dissemination of results

The investigators are committed to the widespread dissemination of the findings of this study. We will seek to publish the results in a peer-reviewed, open access journal, in addition to making the results available to the national and provincial Departments of Health and WHO.

Participant Information Sheet

Department of Obstetrics and Gynaecology,

Frere and Cecilia Makiwane hospitals

To be read by or to each potential participant in her language of choice. One copy of the signed form is to be given to participant.

Screening No: Study ID:

STUDY TITLE: **Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project**

INVESTIGATORS TELEPHONE NUMBERS:

Professor GJ Hofmeyr (Principal Investigator) - 0832809402

To the potential Participant: *Please ask the study staff to explain any words or information in this sheet that you do not clearly understand.*

Good day. My name is ……..…… working at Frere Hospital and/or Cecilia Makiwane Hospital. We wish to give you information about a research study entitled "Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project".

This information sheet is to help you to decide if you would like to take part in this study. You should fully understand what is involved before you agree. If you have any questions, do not hesitate to ask me or the trial staff who will be looking after you.

If you decide to take part in this study, we will ask you to sign a consent form to confirm that you understand what the study involves. We will give you a copy to keep.

WHAT IS THE AIM OF THE STUDY?

Bleeding after birth, also called postpartum haemorrhage, may occur after any birth, though in some cases the risk is higher than usual. Several studies have shown that suction applied inside the uterus with a simple tube designed for other purposes reduces bleeding. In this study a very similar tube but one designed especially for this purpose will be used to prevent excessive bleeding. The overall purpose of the study is to improve the safety of childbirth.

WHAT IS INVOLVED IN THE STUDY?

About 80 participants who give written consent will be included in the study. Of these about 40 will be treated routinely with the suction tube. Another 40 will not be treated routinely, but the suction tube will be available if needed as part of routine care. The choice will be made according to cards which have been prepared in a random order.

After a normal birth, a thin smooth plastic suction tube will be passed through the vagina into the uterus (womb). During a caesarean birth the suction tube will be placed in the uterus and the end passed down through the vagina. In both cases, the tube will be attached to a gentle suction machine for 30 minutes. This method has been shown to help the uterus to contract and thus reduce bleeding. After 30

minutes, if there is no further bleeding, the tube will be removed, but if there is still some bleeding it will be kept in longer.

All women will receive routine care from hospital staff as well as careful monitoring by the research team.

After the birth, we will ask you some questions about how you felt about the care and the procedures. We will also collect information from your medical record.

WHAT ARE THE RISKS OF THE STUDY?

All medical procedures have risks, but we expect that using the suction tube will have more benefit than risk and make the birth safer. Any complications will be treated by the medical team at Frere/Cacilia Makiwane hospitals, and compensation for trial-related complications will be in accordance with the ABPI 2014 guidelines.

WHAT ARE THE BENEFITS OF THE STUDY?

Previous studies have shown that uterine suction is effective for reducing blood loss after birth. All participants in the study will receive close attention and care. The main benefit of being in the study is knowing that you are helping women in the future by providing more accurate information on the usefulness of the specially designed suction tube.

WHAT ARE THE COSTS?

You will not be expected to pay for any study procedures.

WILL I BE PAID?

You will receive a small payment for your time in answering the questionnaire, as determined by the South African Health Products Regulation Authority, of R 400.

HAS THIS STUDY BEEN APPROVED BY AN ETHICS COMMITTEE?

This study has been approved by the Walter Sisulu University Committee for Research on Human Subjects, the Eastern Cape Department of Health Research and Epidemiology Directorate, and the management of Frere and Cecilia Makiwane Hospitals.

The study has been structured in accordance with local and international guidelines for ethical research, including the Declaration of Helsinki, The Department of Health: Ethics in Health Research: Principles Structures and Processes (2nd edition, 2015), and Guidelines for Good Clinical Practice in the Conduct of Clinical Trials in Human Participants in South Africa (2nd Ed.).

WHAT ARE MY RIGHTS?

Taking part in the study is voluntary and you can stop at any time, without stating any reason. This will not result in any penalty or affect your access to medical care.

If you want any more information regarding your rights, or complaints regarding this research study, you may contact chairperson of the Walter Sisulu University Committee for research on human subjects in Mthatha on.

For more information about this study, you can contact Professor Hofmeyr on 0832809402

WHAT ABOUT CONFIDENTIALITY?

All information obtained during the course of this study, including hospital records, personal and research information will be kept strictly confidential. Information that

may be reported in scientific journals will not include any information that identifies you as a participant in this study. Data from the study may be made available to other researchers for further scientific analysis to benefit society. There will be no way of identifying you from the data.

Informed Consent Form

Screening No:

Study ID:

STUDY TITLE: Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project

I, the undersigned, confirm that I have been informed about the procedures, risks, and benefits of the above study. I have read or been read and understood the information sheet provided, and I have been given the opportunity to think about it and ask questions. I understand and agree that the details collected about me and my newborn baby will be stored in a computer and anonymously processed into a report at the end of the study.
Taking part in the study is voluntary. If I take part, I can change my mind and withdraw from the study at any time, and this will not penalise me in any way, or affect the medical care to which I am entitled.
In accordance with the provisions of the Protection of Personal Information Act 4 of 2013 (as amended), I hereby consent:

- To my personal information (hereinafter 'data') being collected, processed, shared and stored in accordance with the research protocol/proposal as approved by the Wits HREC (Medical);
- To my anonymised data being shared, processed, and transferred by third parties and between third parties, and where relevant beyond the jurisdictional borders of South Africa;
- To all findings and results flowing from my anonymised data being broadly shared and published at the conclusion of the research.

I hereby agree to take part in the study.

Notification of my personal doctor:

□YES, I want you to inform my personal doctor of my participation in this study, Dr …….

□NO, I do not want you to inform my personal doctor, or I don't have a personal doctor

…….	…….	…….
Participant Name	Signature	Date and Time
…….	…….	…….
Witness Name	Signature	Date and Time

I, the undersigned, hereby confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

……..	……..	……..
Researcher Name	Signature	Date and Time

Notes or any other comments

Serious adverse event report template

EFFECTIVE CARE RESEARCH UNIT

WORLD HEALTH ORGANIZATION COLLABORATING CENTRE IN RESEARCH SYNTHESIS ON REPRODUCTIVE HEALTH

P/Bag X9047, Frere Maternity Hospital, Amalinda Drive, Selborne, East London, 5201

Cecilia Makiwane Hospital, Mdantsane, East London, 5201

Tel. 27(43)709-2482 E-mail mandisa.singata@gmail.com

Fax 27(43)709-2483 Website www.effectivecareresearch.co.za

The Chair

Human Research Ethics Committee, Walter Sisulu University

Serious adverse event report on our approved protocol M ……..

Study Title Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project

Adverse event report by responsible clinician:

Participant ID:

Adverse event number:

Date of report:

Description of event:

Date of onset:

Date ended:

Severity:

Study intervention: continued/not continued

Participation in study: continued/not continued

Other actions:

Relation of adverse event to intervention (Principal Investigator's assessment):

Case summary:

Additional information from CRF:

Conclusions of study PI:

Reasons:

GJ Hofmeyr

Associate Director: ECRU Date:

ESTA Study Clinical Record Form

Protocol Title: **Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project**		
Site Name:	Subject ID:	Date: (dd/mmm/yy)

Baseline Data (For all data 9,99,999 = unknown)		***Describe**
1. Age (years)	yrs	
2. Previous pregnancies >28 weeks		
3. Previous caesarean sections		
4. Previous PPH. 0 = No 1= Yes		
5. Multiple pregnancy 0 = No 1= Yes		
6. Weight (Kg)		
7. Height (cm)		
8. Pregnancy complications 0 = No 1= Yes*		
9. PPH risk factor(s)*		
10. Mode of delivery: 0=Spont; 1=Assisted; 2=CS;		
11. Reason for CS: 0=PE 1=Fetal distress 2=Breech 3=Prev. CS 4=Poor progress 5=Other*		
12 Baby weight (biggest if twin) (g)		
13. Prophylactic oxytocin 0 = No 1= Yes		
14. Treatment oxytocin* 0 = No 1= Yes		• Before enrolment
15. Treatment ergo- /syntomentrine* 0 = No 1= Yes		
16. Treatment misoprostol* 0 = No 1= Yes		
17. Treatment tranexamic acid* 0 = No 1= Yes		
18. Pre-delivery haemoglobin (g/dL)	.	
Outcome data		**Describe**
	:	
19. Tamponade device inserted?: 0=No; 1=U-STAT; 2=Other tube*; 3=Ellavi; 4 = Other balloon*		
20. Time device inserted:	:	

21. Ease of insertion? 1=easy, 2=mod.diff, 3=difficult		
22. Device stable in uterus? 0=No; 1=Yes		
23. Tube air leak? 0=No; 1=Yes; 3=No tube		
25. Effect of device on exam/mx? 1. Facilitated, 2. Interfered, 3.Neither		
26. Exam obscured by blood from ut: 0=No; 1=Yes		
27. Time bleeding stopped.	:	
28. Time vital signs check (±15min)	:	
29. Syst BP mmHg		
30. Diast BP mmHg		
31. Pulse /m		
32. Additional oxytocin 0 = No 1= Yes		
33. Additional erg- /syntomentrine 0 = No 1= Yes		
34. Additional misoprostol 0 = No 1= Yes		
35. Additional tranexamic acid 0 = No 1= Yes		
36. Time blood collection measured (≥30 min)	:	
37. Blood volume excluding suction jar (ml)		
38. Blood volume in suction jar (ml)		
39. Blood expelled ex ut. after removal of device or after 30 min in control group (ml)		
40. If bleeding persists, measured blood loss post 30min		
41. Laparotomy 0 = No 1= Yes		
42. Compression sutures 0 = No 1= Yes		
43. Uterine devascularization 0 = No 1= Yes		
44. Hysterectomy 0 = No 1= Yes		
45. Other procedure 0 = No 1= Yes*		
46.ICU admission 0 = No 1= Yes		
47. Organ failure 0 = No 1= Yes*		

48. Death 0 = No 1= Yes		
49. Blood transfusion (number of units RBCs)		
50. First Haemoglobin after bleeding controlled (g/dL)		
51. Highest temperature (deg C)		
52. Endometritis 0 = No 1= Yes 9=Unknown		
53. Other complications 0 = No 1= Yes* 9=Unknown		
53. Date of Discharge (DD/MMM/YY)	/ /	

Completed by (initials) :	Date completed (dd/mmm/yy)

Vaginal birth Clinical checklist (remains in hospital records)

Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project

1. ◯ Consent signed
2. ◯ Confirm with Mother that still happy with consent
3. ◯ Study trolley is available with register, U-STAT suction tubes, working suction
4. ◯ Clean drape or Maternawell tray available
5. ◯ Manual suction device ready with vacuum pumped or suction machine pressure set to 100mmHg – block tubing to check
6. ◯ After baby born position drape/Maternawell tray below the buttocks

After placenta delivered completely:

7. ◯ Examine vaginally to exclude major lower genital tract trauma
8. ◯ Note the time, 24 hr: H H : M M
9. ◯ Open next numbered envelope and note allocation: ◯ STUT* ◯ Control
10. ◯ *Insert U-STAT tube to fundus of uterus and start suction
11. ◯ *Insertion of tube; ◯ easy, ◯ moderately difficult, ◯ difficult, ◯ Failed, ◯ not done
12. ◯ Alternative Management ……
13. ◯ *Time tube insertion procedure completed 24 hr: H H : M M
14. ◯ *Check tube/balloon stable in uterus ◯Yes / ◯No / ◯not used
15. ◯ Continue routine care including repair of bleeding tears
16. ◯ *Effect of device on exam/mx of lower genital tract bleeding? ◯Facilitated; ◯Interfered; ◯ Neither; ◯Unknown
17. ◯ Note the time per vaginal bleeding stopped. 24 hr: H H : M M
18. ◯ **15 minutes after insertion** (10 above) note time 24 hr: H H : M M

    Systolic BP ……. Diastolic……. Pulse …….
19. ◯ **30 minutes after insertion**, note time. 24 hr: H H : M M
20. ◯ Measure blood loss in drape/tray = Primary blood loss

				ml
21. ◯ Replace empty tray, expel blood from the uterus by fundal massage (into tray)
22. ◯ Measure blood loss in tray = RESIDUAL

				ml
23. ◯ *disconnect suction. If no bleeding in 10 minutes, remove U=STAT tube
24. ◯ *If bleeding continues, replace empty tray, continue suction plus other measures

25. ◯ When bleeding stopped, measure blood loss in tray = Secondary blood loss

				ml

26. ◯ *Measure blood loss in suction bottle

				ml

27. ◯ *Suction tube problems: ◯ Fell out; ◯ blocked; ◯ leaking; ◯ Poor suction; ◯ None

The participants will be followed till discharge and the outcome data, as well as any complications, recorded.

Caesarean birth Clinical checklist (remains in hospital records)

Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project

1. ◯ Consent signed
2. ◯ Confirm with Mother that still happy with consent
3. ◯ Study trolley is available with register, U-STAT suction tubes, working suction
4. ◯ Clean drape or Maternawell tray available for post-op use
5. ◯ Manual suction device ready with vacuum pumped or suction machine pressure set to 100mmHg – block tubing to check
6. ◯ After birth of baby, open next numbered envelope and note allocation: ◯ STUT* ◯ Control

After placenta delivered completely:

7. ◯ Note the time, 24 hr: H H : M M
8. ◯ *Insert U-STAT tube to fundus of uterus and lower end through cervix and vagina, ask assistant to connect and start suction
9. ◯ *Insertion of tube; ◯ easy, ◯ moderately difficult, ◯ difficult, ◯ Failed, ◯ not done
10. ◯ Alternative Management ……
11. ◯ *Time tube insertion procedure completed 24 hr: H H : M M
12. ◯ Continue uterine closure
13. ◯ *Effect of device on visualisation for uterine closure? ◯Facilitated; ◯Interfered; ◯ Neither; ◯Unknown
14. ◯ Time uterus closed 24 hr: H H : M M
15. ◯ Measure blood volume in suction bottle = pre-suction volume:

				ml

16. ◯ *Note the time bleeding through suction tube stopped. 24 hr: H H : M M
17. ◯ **15 minutes after placental delivery** (7 above) note time 24 hr: H H : M M

    Systolic BP ……. Diastolic……. Pulse …….
18. ◯ After skin closure, estimate surgical blood loss (excluding U=STAT tube drainage)

				ml

19. ◯ In recovery room: Place drape or Maternawell tray under participant's buttocks
20. ◯ *In recovery room: Check tube/balloon stable in uterus ◯Yes / ◯No / ◯not used
21. ◯ **30 minutes after placental delivery** (7 above), note time. 24 hr: H H : M M
22. ◯ Swab vagina and measure blood loss in drape/tray = postop blood blood

				ml

23. ◯ Place new tray or drape under participant and express blood from uterus - Measure blood loss in drape/tray = RESIDUAL blood

				ml

24. ◯ *Disconnect suction, if no bleeding after 10 minutes, remove U-STAT tube. If bleeding resumes, reconnect suction and manage as per hospital protocol
25. ◯ *Measure blood loss in suction bottle

				ml

26. ◯ *Suction tube problems: ◯ Fell out; ◯ blocked; ◯ leaking; ◯ Poor suction; ◯ None

The participants will be followed till discharge and the outcome data, as well as any complications, recorded.

Participant questionnaire (Vaginal birth **Intervention group only**)

Protocol Title: **Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project**		
Site Number:	Subject ID:	Date:(dd/mmm/yy)

Dear Participant, thank you for assisting us with the ESTA project. Pease would you answer the following questions. There are no right or wrong answers. Please just give us your personal opinions. Please feel free not to answer if you prefer not to.

Questionnaire		Comment/Notes
*After the birth of your baby, a tube was inserted to your uterus to help reduce bleeding Please could you describe the pain you experienced? 0=No pain; 1 = Mild pain; 2 = Severe pain; 3 = Unbearable pain; 4 = unsure; 9 = no data		
*Please could you describe how you felt when the tube was removed? 0=No pain; 1 = Mild pain; 2 = Severe pain; 3 = Unbearable pain; 4 = unsure; 9 = no data		
*Please could you describe how you felt overall about the suction tube procedure? 0= fine; 1 = uncomfortable but acceptable; 2 = Unacceptable; 3 = Unbearable; 4 = unsure ; 9 = no data		
Thank you for assisting with this questionnaire		

Completed by (initials) :	Date completed (dd/mmm/yy)

Participant questionnaire (Caesarean birth **Intervention group only**)

Protocol Title: **Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project**		
Site Number:	Subject ID:	Date:(dd/mmm/yy)

Dear Participant, thank you for assisting us with the ESTA project. Pease would you answer the following questions. There are no right or wrong answers. Please just give us your personal opinions. Please feel free not to answer if you prefer not to.

Questionnaire		Comment/Notes
During the caesarean operation, a tube was inserted to your uterus to help reduce bleeding. Please could you describe the pain you experienced from the tube? 0=No pain; 1 = Mild pain; 2 = Severe pain; 3 = Unbearable pain; 4 = unsure; 9 = no data		
Please could you describe how you felt when the tube was removed? 0=No pain; 1 = Mild pain; 2 = Severe pain; 3 = Unbearable pain; 4 = unsure; 9 = no data		
Please could you describe how you felt overall about the suction tube procedure? 0= fine; 1 = uncomfortable but acceptable; 2 = Unacceptable; 3 = Unbearable; 4 = unsure ; 9 = no data		
Thank you for assisting with this questionnaire		

Completed by (initials) :	Date completed (dd/mmm/yy)

Health care provider questionnaire (Vaginal birth **Intervention group only**)

Protocol Title: **Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project**		
Site Number:	Subject ID:	Date:(dd/mmm/yy)

Dear Health care provider, thank you for assisting us with the ESTA project. Pease would you answer the following questions. There are no right or wrong answers. Please just give us your personal opinions. Please feel free not to answer if you prefer not to.

Questionnaire		Comment/Notes
After birth of the baby and placenta, how easy was it to insert the suction tube in the uterus? 0=Easy; 1 = Difficult; 2 = Very difficult; 3 = not possible; 4 = unsure; 9 = no data		
Was the suction tube stable in the uterus? 0=No; 1 = Stable; 2 = fell out; 3 = not used; 4 = unsure; 9 = no data		
Did the suction tube leak air? 0=No; 1 = Leaked a little; 2 = leaked a lot; 3 = not used; 4 = unsure; 9 = no data		
Did the suction tube get blocked? 0=No; 1 = Blocked and cleared; 2 = blocked had to be removed; 3 = not used; 4 = unsure; 9 = no data		
Did the suction tube appear to help with uterine contraction and reducing blood loss? 0=No; 1 = A little; 2 = A lot; 3 = not used; 4 = unsure; 9 = no data		
Was the suction tube easy to remove? 0=easy; 1 = A little difficult; 2 = Very difficult; 3 = not used; 4 = unsure; 9 = no data		
Please could you describe how you felt overall about the suction tube procedure? 0= negative; 1 = Positive; 2 = Neutral; 3 = unsure ; 9 = no data		
Thank you for assisting with this questionnaire		

Completed by (initials) :	Date completed (dd/mmm/yy)

Health care provider questionnaire (Caesarean birth)

Protocol Title: **Equity for Suction Tamponade Access to treat postpartum haemorrhage: The ESTA project**		
Site Number:	Subject ID:	Date:(dd/mmm/yy)

Dear Health care provider, thank you for assisting us with the ESTA project. Pease would you answer the following questions. There are no right or wrong answers. Please just give us your personal opinions. Please feel free not to answer if you prefer not to.		
Questionnaire		Comment/Notes
During the caesarean operation, how easy was it to insert the suction tube in the uterus? 0=Easy; 1 = Difficult; 2 = Very difficult; 3 = not possible; 4 = unsure; 9 = no data		
Did the suction tube help with suctioning blood from the surgical site during closure of the uterus? 0=No; 1 = A little; 2 = A lot; 3 = not used; 4 = unsure; 9 = no data		
After closure of the uterus, did the suction tube seem to help with uterine contraction? 0=No; 1 = A little; 2 = A lot; 3 = not used; 4 = unsure; 9 = no data		
Please could you describe how you felt overall about the suction tube procedure? 0= negative; 1 = Positive; 2 = Neutral; 3 = unsure ; 9 = no data		
Thank you for assisting with this questionnaire		

Completed by (initials) :	Date completed (dd/mmm/yy)

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