ISRCTN16416766 https://doi.org/10.1186/ISRCTN16416766

The carboprost or oxytocin postpartum haemorrhage effectiveness study

Submission date
03/09/2018

Recruitment status
No longer recruiting

Registration date
18/10/2018

Overall study status
Ongoing

Last Edited
12/05/2025

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Excessive bleeding after childbirth (postpartum haemorrhage, PPH) is a common and potentially serious problem affecting 1 in 20 women. Each year it causes 75,000 deaths worldwide. It also causes weakness from anaemia, delayed recovery, psychological trauma, and poor breastfeeding and bonding with their baby. Oxytocin is recommended as first line treatment for PPH as it is low cost, effective and has very few side effects. However, the PPH rate is increasing; laboratory studies suggest that repeated use of oxytocin leads to reduced effectiveness. Carboprost is an alternative treatment and there is evidence that it is more effective than oxytocin, but it is usually reserved for second/third line treatment due to side effects of diarrhoea and vomiting and its cost. The aim of this study is to compare the two drugs, carboprost and oxytocin, currently used to treat PPH, to find out whether it is better to use carboprost or oxytocin as the first drug for treatment for PPH.

Who can participate?
Woman aged 16 and over with PPH

What does the study involve?
Participants are randomly allocated to one of two groups. Two injections are administered. One group receives carboprost and placebo (dummy drug) and the other group receives oxytocin and placebo (dummy drug). There are no extra clinic visits required. Data is collected from medical records. Each participant is followed up 24 hours and 4 weeks later to complete a questionnaire and collect information regarding their healthcare resource use and quality of life. Paper follow-up documents are posted to the homes of participants for their completion.

What are the possible benefits and risks of participating?
The results will help doctors know which treatment is better for PPH treatment. The benefits of participation are that women will receive optimal care, with researchers, clinicians and regulators observing and checking their care carefully so as to ensure that no mistakes are made. This is why clinical outcomes of participants in any study tend to be much better than those of non-participants, irrespective of what treatment they receive. The risks are that of the treatments, both of which are already commonly used as part of PPH management. The common side effects of both treatments are as follows: oxytocin: headache, nausea, vomiting, low blood

pressure, water retention; carboprost: diarrhoea, vomiting, high temperature, increased blood pressure.

Where is the study run from?
Liverpool Women's Hospital (UK)

When is the study starting and how long is it expected to run for?
September 2017 to November 2025

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Miss Charlotte Van Netten
cope@liverpool.ac.uk

Study website
https://www.copestudy.uk

Contact information

Type(s)
Scientific

Contact name
Miss Charlotte Van Netten

Contact details
Liverpool Clinical Trials Centre, University of Liverpool
2nd Floor, Institute in the Park
Alder Hey Children's NHS Foundation Trust
Eaton Road
Liverpool
United Kingdom
L12 2AP
+44 (0)151 795 8760
cope@liverpool.ac.uk

Additional identifiers

EudraCT/CTIS number
2018-001829-11

IRAS number
235254

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

CPMS 39362, IRAS 235254

Study information

Scientific Title
Carboprost vs Oxytocin as the First Line Treatment of Primary Postpartum Haemorrhage: A phase IV, double-blind, double-dummy, randomised controlled trial.

Acronym
COPE

Study objectives
Current study hypothesis as of 07/04/2025:
COPE is a research study to compare the two drugs, carboprost and oxytocin, currently used to treat PPH. About 2000 women will take part across approximately 20 UK NHS hospitals, and we want to know if it is better to use carboprost or oxytocin as the first drug for the treatment of PPH.

Previous study hypothesis:
COPE is a research study to compare the two drugs, carboprost and oxytocin, currently used to treat PPH. About 4000 women will take part across approximately 40 UK NHS hospitals, and we want to know if it is better to use carboprost or oxytocin as the first drug for treatment of PPH.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 04/10/2018, West Midlands - Coventry & Warwickshire Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, BG1 6FS, United Kingdom; +44 2071048009; coventryandwarwick.rec@hra.nhs.uk), ref: 18/WM/0227

Study design
Randomized; Both; Design type: Treatment, Drug, Qualitative

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied

Postpartum haemorrhage

Interventions

Current interventions as of 07/04/2025:
COPE aims to recruit 2000 women across 20 UK hospitals via two recruitment pathways:
1. Women at high risk of PPH (defined as relative risk of > 3) will be invited to prospectively consent to participation within COPE and will be approached antenatally by a COPE recruiter who will provide information and the opportunity for discussion. At this point, women will have the opportunity to decline participation in the study, in which case a ""COPE declined"" sticker will be placed in the woman's case notes.
2. Women at low risk of PPH who meet eligibility criteria will be randomised into the trial in the emergency situation, where treatment needs to be given urgently and there is no time for prior consent. Postnatally, full study information will be provided and the woman will be asked to sign the emergency consent form. In the event that capacity is not regained or delayed, a personal or professional legal representative will be approached for informed emergency consent.

Participants will be randomised in a 1:1 ratio using random variable block size, stratified by mode of birth (caesarean section or vaginal birth) to one of the following treatment arms:
Intervention: Carboprost 250 micrograms by deep intramuscular injection and 1ml placebo by slow intravenous injection.
Control: Oxytocin 10 international units by slow intravenous injection and 1ml placebo by deep intramuscular injection.

Centres will be provided with a series of sequentially numbered, sealed treatment kits to be received by the pharmacy department and distributed to an appropriate secure location within the delivery suite for ready access upon presentation of eligible patients. A placebo vial will be administered intravenously alongside carboprost and intramuscularly alongside oxytocin in order to conserve the blinding of treatments for both healthcare professionals and participants. This will eradicate any potential bias.

The design of this study has been developed to have minimal impact on families, resulting in the need for no extra clinic visits within the trial. Clinical outcome data will be collected from medical records. Each participant will be followed up at 24 hours and 4 weeks post randomisation to obtain data for the childbirth experience questionnaire, and information regarding their resource use and quality of life, where applicable. Such follow-up documents will be paper based and posted to the homes of participating women for their completion.

At the time of consent to the main study, participants will also be invited to take part in an embedded study, including;
1. Audio recording of COPE antenatal consent discussions between women and their birth partner (if applicable) and trial recruiters
2. Interviews with women and their birth partners (if applicable) who agree or decline consent including bereaved women; either by telephone or at an agreed location
3. A questionnaire for both women who agree or decline consent to the main trial
4. Focus groups and/or interviews with COPE trial recruiters at each pilot site

Previous interventions:
COPE aims to recruit 3,948 women across 40 UK hospitals via two recruitment pathways:
1. Women at high risk of PPH (defined as relative risk of > 3) will be invited to prospectively consent to participation within COPE and will be approached antenatally by a COPE recruiter who will provide information and the opportunity for discussion. At this point, women will have the opportunity to decline participation in the study, in which case a ""COPE declined"" sticker

will be placed in the woman's case notes.
2. Women at low risk of PPH who meet eligibility criteria will be randomised into the trial in the emergency situation, where treatment needs to be given urgently and there is no time for prior consent. Postnatally, full study information will be provided and the woman will be asked to sign the emergency consent form. In the event that capacity is not regained or delayed, a personal or professional legal representative will be approached for informed emergency consent.

Participants will be randomised in a 1:1 ratio using random variable block size, stratified by mode of birth (caesarean section or vaginal birth) to one of the following treatment arms:
Intervention: Carboprost 250 micrograms by deep intramuscular injection and 1ml placebo by slow intravenous injection.
Control: Oxytocin 10 international units by slow intravenous injection and 1ml placebo by deep intramuscular injection.

Centres will be provided with a series of sequentially numbered, sealed treatment kits to be received by the pharmacy department and distributed to an appropriate secure location within the delivery suite for ready access upon presentation of eligible patients. A placebo vial will be administered intravenously alongside carboprost and intramuscularly alongside oxytocin in order to conserve the blinding of treatments for both healthcare professionals and participants. This will eradicate any potential bias.

The design of this study has been developed to have minimal impact on families, resulting in the need for no extra clinic visits within the trial. Clinical outcome data will be collected from medical records. Each participant will be followed up at 24 hours and 4 weeks post randomisation to obtain data for the childbirth experience questionnaire, and information regarding their resource use and quality of life, where applicable. Such follow-up documents will be paper based and posted to the homes of participating women for their completion.

At the time of consent to the main study, participants will also be invited to take part in an embedded study, including;
1. Audio recording of COPE antenatal consent discussions between women and their birth partner (if applicable) and trial recruiters
2. Interviews with women and their birth partners (if applicable) who agree or decline consent including bereaved women; either by telephone or at an agreed location
3. A questionnaire for both women who agree or decline consent to the main trial
4. Focus groups and/or interviews with COPE trial recruiters at each pilot site

Intervention Type
Other

Phase
Phase IV

Primary outcome measure
Blood transfusion - any RBC blood transfusion or cell salvage of ≥ 300ml commenced any time between randomisation and 48 hours after randomisation (or hospital discharge if earlier than 48 hrs), measured using medical notes

Secondary outcome measures
1. Volume of blood transfusion from randomisation up to 48 hours (or hospital discharge if earlier), measured using medical notes

2. Use of a further uterotonic drug from randomisation up to 24 hours after randomisation, measured using medical notes
3. Composite outcome of any organ dysfunction based on WHO near-miss approach for maternal health (2) from randomisation up to hospital discharge (or 4 weeks whichever is earlier)
4. Hysterectomy from randomisation up to hospital discharge (or 4 weeks whichever is earlier) , measured using medical notes
5. Blood loss in ml commencing in the first 24 hours from randomisation, up to cessation of active bleeding, measured using medical notes
6. Blood loss ≥ 1000 ml, measured using medical notes
7. Haemoglobin closest to 24 hours after randomisation, measured using medical notes
8. Shock within 24 hours of randomisation, measured using medical notes
9. Maternal death within 4 weeks of the birth where postpartum haemorrhage was a contributing factor (it does not need to be the primary cause), measured using medical notes
10. Non pharmacological approach to treat or investigate bleeding from randomisation up to hospital discharge, measured using medical notes
11. Manual removal of placenta post randomisation up to hospital discharge, measured using medical notes
12. Any adverse reactions of the intervention for the mother (hypotension occurring within 2 mins of IMP administration, all other adverse reactions occurring within 2 hrs of administration) , measured using medical notes
13. 'Skin to skin' care with baby within the first hour after birth, measured using medical notes
14. Separation from new-born in first hour after birth, measured using medical notes
15. Breastfeeding, measured using [method] at 24 hrs, 48 hrs (or hospital discharge if sooner) and 4 weeks
16. Woman's experience, measured using Childbirth Experience Questionnaire (CEQ) at 4 weeks
17. Resource use, measured using EQ-5D-5L, resource use questionnaire and hospital episode statistics at 24 hrs and 4 weeks

Overall study start date
01/09/2017

Completion date
28/11/2025

Eligibility

Key inclusion criteria
1. ≥16 years of age
2. Requirement for medical treatment for primary PPH

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Female

Target number of participants
Planned Sample Size: 2000; UK Sample Size: 2000

Key exclusion criteria
Current participant exclusion criteria as of 28/03/2025:
1. Known to have opted out of participation antenatally
2. Known oxytocin or carboprost hypersensitivity
3. Known active cardiac or pulmonary disease
4. Known to have previously been treated as part of COPE
5. Has already received carboprost prophylactically for postpartum haemorrhage
6. Has already received uterotonic drug treatment for postpartum haemorrhage (this does not include PPH prophylaxis)
7. Stillbirth

Previous participant exclusion criteria:
1. Known to have opted out of participation antenatally
2. Known oxytocin or carboprost hypersensitivity
3. Known active cardiac or pulmonary disease
4. Known to have previously been treated as part of COPE
5. Has already received uterotonic drug treatment for postpartum haemorrhage (this does not include PPH prophylaxis)
6. Stillbirth

Date of first enrolment
01/11/2020

Date of final enrolment
31/05/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Liverpool Women's Hospital
Crown Street
Liverpool
United Kingdom
L8 7SS

Study participating centre
Birmingham Women's Hospital
Mindelsohn Way

Edgbaston
Birmingham
United Kingdom
B15 2TG

Study participating centre
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
University College Hospital
235 Euston Road
London
United Kingdom
NW1 2BU

Study participating centre
Burnley General Hospital
Casterton Avenue
Burnley
United Kingdom
BB10 2PQ

Study participating centre
Kingston Hospital
Galsworthy Road
Kingston upon Thames
United Kingdom
KT2 7QB

Study participating centre
The Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
TS1 4LP

Study participating centre
University Hospital of North Tees
Hardwick Road
Stockton-on-tees
United Kingdom
TS19 8PE

Study participating centre
Whittington Health NHS Trust
The Whittington Hospital
Magdala Avenue
London
United Kingdom
N19 5NF

Study participating centre
Gateshead Hospitals NHS Trust
Queen Elizabeth Hospital
Sherriff Hill
Gateshead
United Kingdom
NE9 6SX

Study participating centre
Medway NHS Foundation Trust
Medway Maritime Hospital
Windmill Road
Gillingham
United Kingdom
ME7 5NY

Study participating centre
Poole
Poole Hospital
Longfleet Road
Poole
United Kingdom
BH15 2JB

Study participating centre

John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Nottingham University Hospitals NHS Trust - City Campus
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Kings College Hospital
Mapother House
De Crespigny Park
Denmark Hill
London
United Kingdom
SE5 8AB

Study participating centre
Princess Royal University Hospital
Farnborough Common
Orpington
United Kingdom
BR6 8ND

Study participating centre
Queens Medical Centre, Nottingham University Hospital
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
West Wales General Hospital
Dolgwili Road

Carmarthen
United Kingdom
SA31 2AF

Study participating centre
North Tyneside General Hospital - Valneva Covid19 Trials
North Tyneside General Hospital
Rake Lane
North Shields
United Kingdom
NE29 8NH

Study participating centre
Musgrove Park Hospital (taunton)
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Sponsor information

Organisation
University of Liverpool

Sponsor details
c/o Mr Alex Astor
Address Research Support Office
2nd Floor Block D Waterhouse Building
3 Brownlow Street
Liverpool
England
United Kingdom
L69 3GL
+44 (0)1517948739
sponsor@liverpool.ac.uk

Sponsor type
University/education

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 16/16/06

Results and Publications

Publication and dissemination plan
Protocol will be made available at a later date. Planned publication of the results in a high-impact peer reviewed journal.

Intention to publish date
28/05/2026

Individual participant data (IPD) sharing plan
1. The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository
2. The datasets generated during and/or analysed during the current study are/will be available upon request

IPD sharing plan summary
Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v2.0	26/09/2018	02/04/2019	No	Yes
Participant information sheet	version v2.0	26/09/2018	02/04/2019	No	Yes
HRA research summary			28/06/2023	No	No
Participant information sheet	version 9.0	05/03/2024	28/03/2025	No	Yes
Protocol file	version 8.0	06/03/2024	28/03/2025	No	No
Protocol article		08/05/2025	12/05/2025	Yes	No