

# The carboprost or oxytocin postpartum haemorrhage effectiveness study

<b>Submission date</b> 03/09/2018	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 18/10/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 21/11/2025	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Miss Charlotte Van Netten

**Contact details**  
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Liverpool  
United Kingdom  
L12 2AP  
+44 (0)151 795 8760  
cope@liverpool.ac.uk

## Additional identifiers

**Integrated Research Application System (IRAS)**  
235254

**Central Portfolio Management System (CPMS)**  
39362

## 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

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### 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

### Study type(s)

Treatment

### 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.

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## **Intervention Type**

Other

## **Primary outcome(s)**

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

## **Key secondary outcome(s)**

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  $\geq 1000$  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

**Completion date**

28/11/2025

## Eligibility

**Key inclusion criteria**

- 1.  $\geq 16$  years of age
- 2. Requirement for medical treatment for primary PPH

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

16 years

**Upper age limit**

99 years

**Sex**

Female

**Total final enrolment**

2058

**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**

United Kingdom

England

**Study participating centre**

**Liverpool Women's Hospital**

Crown Street

Liverpool

England

L8 7SS

**Study participating centre**

**Birmingham Women's Hospital**

Mindelsohn Way

Edgbaston

Birmingham

England

B15 2TG

**Study participating centre**

**Sunderland Royal Hospital**

Kayll Road

Sunderland

England

SR4 7TP

**Study participating centre**  
**University College Hospital**  
235 Euston Road  
London  
England  
NW1 2BU

**Study participating centre**  
**Burnley General Hospital**  
Casterton Avenue  
Burnley  
England  
BB10 2PQ

**Study participating centre**  
**Kingston Hospital**  
Galsworthy Road  
Kingston upon Thames  
England  
KT2 7QB

**Study participating centre**  
**The Royal Victoria Infirmary**  
Queen Victoria Road  
Newcastle upon Tyne  
England  
TS1 4LP

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

**Study participating centre**  
**Whittington Health NHS Trust**  
The Whittington Hospital  
Magdala Avenue



London  
England  
N19 5NF

**Study participating centre**  
**Gateshead Hospitals NHS Trust**  
Queen Elizabeth Hospital  
Sherriff Hill  
Gateshead  
England  
NE9 6SX

**Study participating centre**  
**Medway NHS Foundation Trust**  
Medway Maritime Hospital  
Windmill Road  
Gillingham  
England  
ME7 5NY

**Study participating centre**  
**Poole**  
Poole Hospital  
Longfleet Road  
Poole  
England  
BH15 2JB

**Study participating centre**  
**John Radcliffe Hospital**  
Headley Way  
Headington  
Oxford  
England  
OX3 9DU

**Study participating centre**  
**Nottingham University Hospitals NHS Trust - City Campus**  
Nottingham City Hospital  
Hucknall Road  
Nottingham

England  
NG5 1PB

**Study participating centre**

**Kings College Hospital**

Mapother House  
De Crespigny Park  
Denmark Hill  
London  
England  
SE5 8AB

**Study participating centre**

**Princess Royal University Hospital**

Farnborough Common  
Orpington  
England  
BR6 8ND

**Study participating centre**

**Queens Medical Centre, Nottingham University Hospital**

Derby Road  
Nottingham  
England  
NG7 2UH

**Study participating centre**

**West Wales General Hospital**

Dolgwili Road  
Carmarthen  
Wales  
SA31 2AF

**Study participating centre**

**North Tyneside General Hospital - Valneva Covid19 Trials**

North Tyneside General Hospital  
Rake Lane  
North Shields  
England  
NE29 8NH

**Study participating centre**  
**Musgrove Park Hospital (taunton)**  
Musgrove Park Hospital  
Taunton  
England  
TA1 5DA

## Sponsor information

**Organisation**  
University of Liverpool

**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

### 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

Available on request, Stored in non-publicly available repository

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	version v2.0	08/05/2025	12/05/2025	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>		26/09/2018	02/04/2019	No	Yes

<a href="#">Participant information sheet</a>	version v2.0	26/09/2018	02/04/2019	No	Yes
<a href="#">Participant information sheet</a>	version 9.0	05/03/2024	28/03/2025	No	Yes
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Protocol file</a>	version 8.0	06/03/2024	28/03/2025	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes