UNIVERSITY OF MALAYA MEDICAL CENTRE

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UNIVERSITY OF MALAYA

*The Leader in Research & Innovation*

RESEARCH PROPOSAL FOR MASTER OF MEDICINE
(OBSTETRICS AND GYNAECOLOGY)
DEPARTMENT OF OBSTETRICS & GYNAECOLOGY
UNIVERSITY OF MALAYA

# INTRAMUSCULAR OXYTOCIN 10 IU AND ORAL MISOPROSTOL 600 MCG VERSUS INTRAMUSCULAR FIXED DOSE OXYTOCIN 5 IU AND ERGOMETRINE 500 MCG AND ORAL PLACEBO PROPHYLAXIS FOLLOWING A VAGINAL DELIVERY: A RANDOMISED CONTROLLED TRIAL

**RESEARCH PROPOSAL**

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BY

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## CHAPTER 1 : INTRODUCTION

Worldwide, postpartum hemorrhage (PPH) accounts for 8% of maternal deaths in developed regions of the world and 20% of maternal deaths in developing regions.[1,2] PPH can also lead to severe anemia requiring blood transfusion, disseminated intravascular coagulopathy, hysterectomy and multisystem organ failure.[3]

The traditional definition of PPH is blood loss of more than 500 ml after a vaginal delivery or more than 1000 ml after a cesarean delivery but more recently, postpartum hemorrhage has been redefined as a cumulative blood loss of 1000 ml or more or blood loss associated with signs or symptoms of hypovolemia, irrespective of the route of delivery.[3] The most common cause is uterine atony (accounting for approximately 70% of cases), followed by obstetrical lacerations (approximately 20%), retained placental tissue (approximately 10%), and clotting-factor deficiencies (<1%).[3] PPH is considered primary within the first 24 hours after delivery and secondary between 24 hours and up to 12 weeks after delivery.[4]

Oxytocin (10 IU, intravenously or intramuscularly) for the prevention of PPH is recommended by the World Health Organisation (WHO)[5] and national guidelines.[6] WHO also recommends that where oxytocin is unavailable, the use of the fixed drug combination of oxytocin and ergometrine or oral misoprostol (600 µg) is recommended.[5] In our center the first line drug for PPH prevention after vaginal delivery was combination oxytocin and ergometrine (Syntometrine), which is one of the two agents suggested by Malaysian guideline.[7]

A network meta-analysis on uterotonic drugs to prevent PPH shows that ergometrine plus oxytocin has risk ratio (RR) 0.69, carbetocin RR 0.72 and misoprostol plus oxytocin RR 0.73 for PPH blood loss of ≥ 500 ml compared with oxytocin as referent. Oxytocin was ranked fourth, with an almost 0% cumulative probability of being ranked in the top three.[8] Data from a recent landmark trial that compared carbetocin to oxytocin for PPH prevention

after vaginal birth, shows that carbetocin was only noninferior to oxytocin for the prevention of blood loss of ≥500 ml or the use of additional uterotonic agents and was not noninferior even for blood loss of ≥1000 ml.[9] These data taken as a whole support combinations of ergometrine plus oxytocin and misoprostol plus oxytocin as the most effective for PPH prevention.[8,10]

However, to treat postpartum haemorrhage, a network meta-analysis on first line uterotonic drugs shows that misoprostol alone as first-line treatment uterotonic agent, probably increases the risk of blood transfusion compared with oxytocin and may also increase the incidence of additional blood loss of ≥1000 ml.[11]

Oxytocin has a plasma half-life of 6 min 53 s in female serum[12,13], misoprostol after oral administration has a time to maximum plasma concentration of 12 minutes and a terminal half-life of 20–40 minutes[14] and ergometrine has terminal half-life of 1.86 hours.[15,16] The very short half-life for oxytocin provide a rationale for its combination with ergometrine or misoprostol to provide for a more prolonged uterotonic effect as primary PPH can occur within the first 24 hours after delivery.[4]

Oxytocin is the most widely used uterotonic drug. At higher dosages, it causes sustained tetanic uterine contractions. When used intramuscularly, the latent phase lasts 2–5 minutes. Oxytocin is unstable at room temperature and it requires cold storage and transport.[17] Misoprostol is a prostaglandin E1 analogue is well known for its off-label use as a uterotonic agent. The half-life is about 20–40 minutes.[17] Misoprostol onset of action after oral intake is 8 min and its duration of action is 2 hours. It is water-soluble and heat stable.[18] Ergometrine is an ergot alkaloid that increases uterine muscle tone by causing sustained uterine contractions. After IM injection, it has a latent phase of 2–5 minutes. It is unstable in heat, and is vasoconstrictive.[17]

Combinations of ergometrine plus oxytocin or misoprostol plus oxytocin cause significantly more side effects compared to oxytocin alone.[10] Based on network meta-analysis findings, compared to oxytocin, ergometrine has RR 8.5: and misoprostol RR 1.5 for hypertension:, ergometrine has RR 0.77 and misoprostol RR 3.87 for fever and ergometrine has RR 2.36 and misoprostol RR 1.63 for vomiting.[10] These findings appear to show especially large and contrasting difference in the side effects of hypertension and fever that is plausible between the drug combinations.

Combination ergometrine plus oxytocin (syntometrine) is contraindicated when hypertension is present.[19] Hypertensive disorders in pregnancy has a global prevalence of 5.2–8.2%.[20] NHS (National Health Service) England has identified an issue with syntometrine being administered when contraindicated in women with significantly raised blood pressure, noting that current UK 'national guidance recommends that oxytocin alone, rather than syntometrine, is administered to help deliver the placenta, but a review of similar incidents showed that this is not being reflected in local practices'.[21] Syntometrine use for primary prevention of PPH appears to be not insignificant in UK practice [21] and also in Malaysian practice.[7]

Data is lacking on a head to head trial of ergometrine plus oxytocin compared to misoprostol plus oxytocin used for PPH prevention in vaginal delivery. We plan to perform a randomized trial predicated primarily on tolerability (hypertension and fever) of these drug combinations.

## CHAPTER 2 : OBJECTIVES AND HYPOTHESIS

### 2.1 Research Objectives

To compare tolerability and effectiveness of oxytocin 10 IU i.m. plus oral misoprostol 600 mcg to syntometrine i.m. (fixed dose oxytocin 5 IU plus ergometrine 0.5mg) plus oral placebo when used following a vaginal delivery for first line postpartum hemorrhage prevention.

Primary outcomes

1) Hypertension (systolic ≥ 140 mmHg and/or diastolic ≥ 90 mmHg)
2) Fever (≥ 37.5 $^{0}$C)

at 1 hour after delivery

Secondary outcomes[22]

1) Blood loss

   • Total blood loss will be determined by calculated EBL (cEBL)[23]

   - Calculated pregnancy blood volume = (0.75 ([maternal height (inches) X 50]+ [maternal weight in pounds X 25])

   - Percent of blood volume lost = (Predelivery HCT- postdelivery HCT) / predelivery HCT.

   - Calculated estimated blood loss (cEBL) = Calculated pregnancy blood volume X Percent of blood volume lost

2) Use of additional haemostatic intervention (including uterotonics, operative interventions) ascertained at hospital discharge from EMR
3) Transfer for higher level of care (HDU or ICU) ascertained at hospital discharge
4) Blood transfusion ascertained at hospital discharge from EMR
5) Women's sense of wellbeing (0-10 NRS) ascertained before hospital discharge

6) Satisfaction with the intervention (0-10 NRS) ascertained before hospital discharge
7) Breastfeeding (time to first satisfactory breastfeeding from maternal perspective) time and date recorded at first satisfactory breastfeeding
8) Shock[24] ascertained at hospital discharge from EMR
9) Coagulopathy ascertained at hospital discharge from EMR
10) Hysterectomy ascertained at hospital discharge from EMR
11) Organ dysfunction ascertained at hospital discharge from EMR
12) Maternal death ascertained from EMR
13) Adverse effects (cumulative, ascertained at 6 hours after delivery) before hospital discharge from EMR
    a. hypertension
    b. fever
    c. vomiting
    d. shivering
    e. epigastric discomfort or fullness
    f. diarrhoea
    g. headache
    h. chest pain
    i. palpitation
    j. shortness of breath
14) Composite adverse effects of at least one of hypertension, fever, vomiting, shivering, epigastric discomfort or fullness, diarrhoea, headache, chest pain, palpitation, shortness of breath
15) Major harms
    a. Haemorrhagic cerebral vascular event due to hypertension

b. Maternal febrile convulsion

c. Maternal ICU admission for bleeding complications due to uterine atony

## 2.2 Clinical Rationale & Objectives

To prevent postpartum haemorrhage (PPH), a network meta-analysis on uterotonic drugs shows that ergometrine plus oxytocin has risk ratio (RR) 0.69 and misoprostol plus oxytocin RR 0.73 for PPH ≥ 500 ml compared with oxytocin as the referent drug.[8]

Based on network meta-analysis findings, compared to oxytocin, ergometrine has RR 8.5: and misoprostol RR 1.5 for hypertension, ergometrine has RR 0.77 and misoprostol RR 3.87 for fever and ergometrine has RR 2.36 and misoprostol RR 1.63 for vomiting.[10] These findings appear to show especially large and contrasting difference in the side effects of hypertension and fever, and a smaller difference against ergometrine on vomiting with these drug combinations.

A head to head comparison of ergometrine plus oxytocin versus misoprostol plus oxytocin for PPH prevention in vaginal delivery has not been explored.

In UMMC the standard PPH prevention in vaginal delivery is Syntometrine® (fixed dose oxytocin 5 IU and ergometrine 0.5mg). Syntometrine should not be administered when there is high blood pressure. However, pre-eclampsia can and do arise by stealth and without warning after delivery and the syntometrine administered immediately at childbirth may inadvertently coincide with and potentially worsen the new onset hypertension of pre-eclampsia. With this coincidence severe complications such as cerebral vascular haemorrhage and convulsion due to severe hypertension may theoretically occur but they are likely to be extremely rare events which are not expected to occur within this study.

Objective: To compare tolerability and effectiveness of oxytocin 10 IU i.m. plus oral misoprostol 600 mcg to syntometrine i.m. (fixed dose oxytocin 5 IU and ergometrine 0.5mg) plus oral placebo when used following a vaginal delivery for first line PPH prevention

Expected outcomes: Oxytocin 10 IU i.m. plus oral misoprostol 600 mcg compared to syntometrine i.m. plus oral placebo could be associated with lower occurrences of hypertension and vomiting but higher occurrences of fever at 1 hour after delivery with similar effect on PPH.

**2.3 Research Hypothesis**

We hypothesize that oxytocin 10 IU i.m. plus oral misoprostol 600 mcg compared to syntometrine i.m. plus oral placebo would be associated with lower occurrences of hypertension and higher occurrences of fever at 1 hour after delivery.

# CHAPTER 3 : METHODOLOGY

## 3.1 Study type and design

A single blind parallel group randomised trial.

## 3.2 Study Area

Labour ward, University Malaya Medical Centre (UMMC).

## 3.3 Duration of Study

This study will be conducted over a period of 10 months ( March 2024 till December 2024).

## 3.4 Ethical consideration

Ethical approval will be obtained from the Ethics Committee of University of Malaya Medical Centre. The study will be conducted in full compliance with the principles proclaimed in the Declaration of Helsinki on human research. Written informed consent will be obtained from all participants. This study will also be registered with ISRCTN.

## 3.5 Sample size

The two prespecified primary outcomes were hypertension and fever at 1 hour after delivery. To our best knowledge, a head to head trial of ergometrine plus oxytocin compared to misoprostol plus oxytocin for PPH prevention in vaginal delivery is not available to derive pilot data for sample size calculation. Based on network meta-analysis findings, compared to oxytocin, ergometrine has RR 8.5 and misoprostol RR 1.5 (derived ergometrine to misoprostol RR 5.67 [8.5/1.5]) for hypertension and ergometrine has RR 0.77 and misoprostol RR 3.87 (derived ergometrine to misoprostol RR 0.20 [0.77/3.87]) for fever as side effects[10].

1) Hypertension: assuming a baseline hypertension rate of 5% with misoprostol applying a conservative RR 2.5 (instead of RR 5.57), alpha 0,05, beta 0.8, 1 to 1 ratio. Chi Square test using Power and Sample Size Program[25], 222 women are needed in each arm.
2) Fever: assuming a baseline fever rate of 5% with misoprostol applying a conservative RR 0.3 (instead of RR 0.2), alpha 0,05, beta 0.8, 1 to 1 ratio. Chi Square test using Power and Sample Size Program(19), 402 women are needed in each arm.

Taking into account a 10% dropout rate (402x2)/0.9=893.3 participants, rounded up to a total 900 are needed (450 in each arm).

**3.6 Statistical Analysis**

Data will be entered into a statistical software package SPSS (Version 26, IBM, SPSS Statistic). Normality of distribution of continuous data distribution will be assessed with the Kolmogorov-Smirnov test. The Student t-test will used to analyze continuous data with normal data distribution, the Mann-Whitney U test for non-normally distributed data or ordinal data and Chi-square test for categorical data (Fisher exact test if ⩾20% of cells had cell number <5). Two-sided P values will be reported: $P < 0.05$ will be regarded as significant. Analysis will be on intention-to-treat basis.

**3.7 Inclusion criteria:**

- Expecting a vaginal delivery
- Age 18-45 years
- Term gestation (≥37weeks)
- Single fetus
- Cephalic presentation
- Parity <5

- Final inclusion for randomization: have achieved vaginal delivery

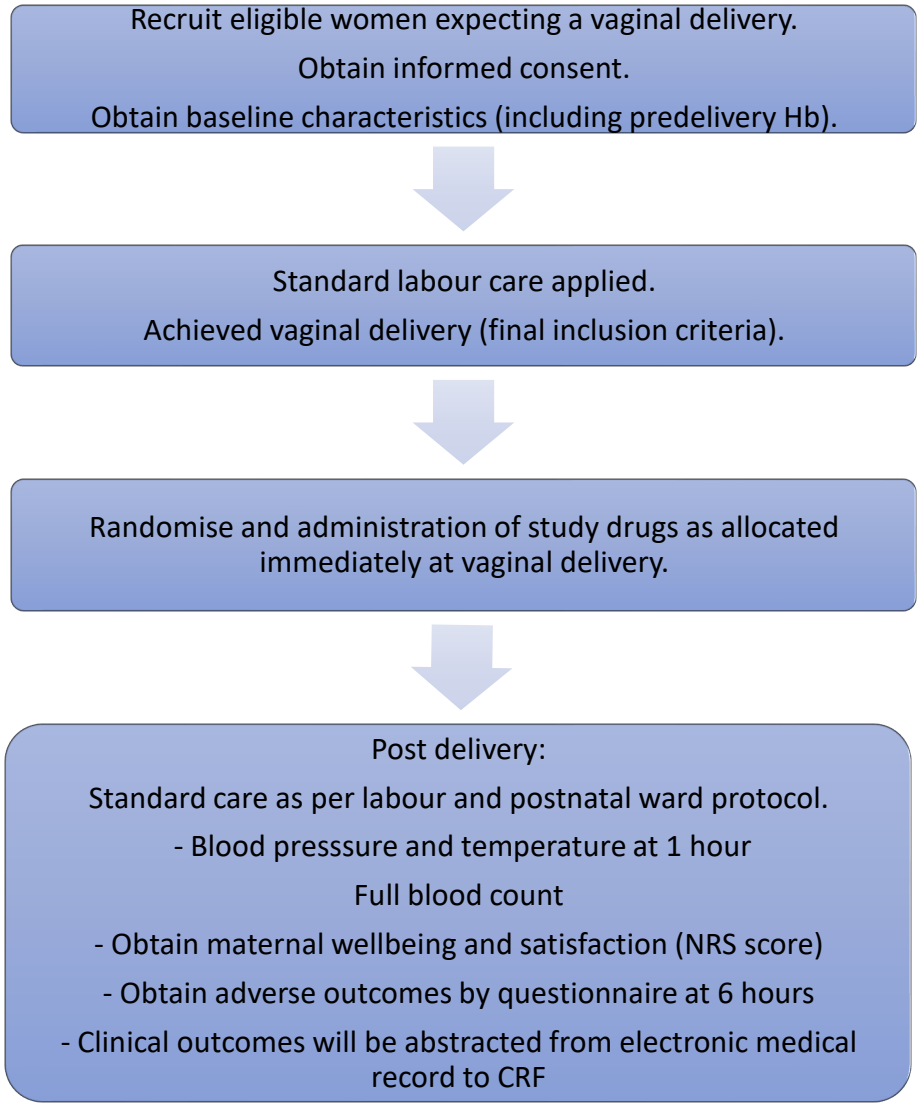
**3.8 Exclusion criteria:**

- Woman with any contraindication for the use of oxytocin, misoprostol and ergometrine
- Known case of hypertensive, cardiovascular, hepatic or hematologic disorders

**3.9 Study Flow / Procedures**

- Patient recruitment will take place in antenatal or labour ward of UMMC
- All women expecting a vaginal delivery will be assessed for eligibility.
- Those who fulfilled the eligible criteria will be provided with patient information sheet.
- Oral queries will be invited of potential recruits and answered by recruiter
- Written informed consent will be taken from all who agree to participate.
- Patients will be randomized to 2 groups of treatment after vaginal delivery

**Schematic diagram of the study design**




- Interventions

At the delivery of the anterior shoulder or latest before delivery of the placenta,

i) will receive i.m. oxytocin 10IU plus oral misoprostol 600 mcg

or

ii) will receive i.m. syntometrine (fixed dose oxytocin 5 IU and ergometrine 500mcg) plus oral placebo

These prepared interventions will be placed in the sealed opaque numbered randomization envelopes.

**Study drugs**

Misoprostol

Misoprostol is a prostaglandin E1 analogue that is licensed for the prevention and treatment of gastric ulcers. It is widely used off-label as a uterotonic agent. The half-life is about 20–40 minutes.[17] Misoprostol onset of action after oral intake is 8 min and its duration of action is 2 hours. It is water-soluble and heat stable.[18]

Oxytocin

Oxytocin is the most widely used uterotonic drug. At higher dosages, it causes sustained tetanic uterine contractions. When used intramuscularly, the latent phase lasts 2–5 minutes. Oxytocin is unstable at room temperature and it requires cold storage and transport.[17] Plasma half-life is 6 min 53 s in female serum.[12,13]

Ergometrine

Ergometrine is an ergot alkaloid that increases uterine muscle tone by causing sustained uterine contractions. After IM injection, it has a latent phase of 2–5 minutes. The plasma half-life is 30–120 minutes. It is unstable in heat, and is vasoconstrictive.[17]

Randomization

Randomization will be performed and intention to treat revealed only after successful vaginal delivery. Randomization is done by opening the lowest number, sealed and opaque envelope that is available. Randomization sequence will be generated using random number generator in random blocks of 4 or 8 by an investigator who is not involved in recruitment.

Blinding

3x 200mcg misoprostol and 3 similar looking inert placebo tablets will be used. Numbered envelopes will be packed with oxytocin ampoule plus 3 misoprostol tablets or syntometrine ampoule plus 3 inert tablets as randomly allocated.

Rescue therapy for bleeding, hypertension, and fever

Suggested rescue therapies

A) Vaginal bleeding due to uterine atony (medical rescue)

    a. Unresolved blood loss ≥ 1000ml, stat slow bolus intravenous tranexamic acid 1g in 10 ml over 1-2 minutes

    Uterotonics

    b. Intravenous oxytocin infusion 40 i.u. in 500 ml Hartmann solution over 4-8 hours, if insufficient effect then
    c. Carboprost 250 mcg i.m. stat, (May be repeated every 15-90-min. Max: 2 mg - 8 x 250 mcg doses), if insufficient effect then
    d. Consider bolus i.v. oxytocin 5 i.u., ergometrine 500 mg i.m. (or syntometrine) or per rectal misoprostol 800 mcg stat

    Care provider should apply their usual rescue therapy for failed primary prophylaxis of PPH if more comfortable and experienced with it.

B) Hypertension (new onset)

a. Consider pre-eclampsia and if index suspicion is high, manage as for post-delivery pre-eclampsia

Hypertension suspected to be due to study medication

b. Non-severe hypertension systolic BP < 160 and diastolic BP < 110 mmHg, observe every 30 minutes

c. Severe hypertension systolic BP ≥160 and/or diastolic BP ≥ 110 mmHg, oral nifedipine 10 mg stat (non-slow release preparations), and repeat every 15 minutes if severe hypertension persists and observe every 30 minutes once hypertension is no longer severe and deescalating as normally warranted.

Hypertensive effects from study medication is not anticipated 6 hours after administration.

C) Fever (new onset)

a. Consider infective aetiology and if index of suspicion is high, manage for most likely origin of infection clinically

Fever suspected to be due to study medication

b. If temperature ≥ 37.5 $^{0}$C, oral paracetamol 1 g if not already administered for analgesia

c. Consider ibuprofen 400 mg instead of or in additional to paracetamol as needed

d. Tepid sponging if temperature ≥ 39.0 $^{0}$C

Fever from study medication is not anticipated 6 hours after administration.

Stopping rules for the study participants

The study interventions are both solitary bolus treatments (an intramuscular injection and a concurrent oral capsule in both arms). A stopping rule is not applicable as there is no

continuing therapy to terminate.

Discontinuation criteria for the study

The study will be immediately paused in the event of specified major harms of

a. Haemorrhagic cerebral vascular event due to hypertension
b. Maternal febrile convulsion
c. Maternal ICU admission for bleeding complications due to uterine atony

The matter will be brought to the attention of department safety monitoring subcommittee for immediate consideration. The study will only continue once approval to restart is obtained from a responsible oversight body.

Post-birth Monitoring and Assessments

A) Post-delivery labour ward and postnatal monitoring

1) Blood pressure measurement hourly on indicated labour ward stay until decision to dispatch to postnatal ward and on arrival at postnatal ward then every 4 hours until deescalated as clinically warranted

2) Temperature will be taken at 1 hour post-delivery, 4 hours later then daily until deescalated as clinically warranted

3) Clinical assessment of blood loss at delivery, hourly on indicated labour ward stay, on arrival at postnatal ward then daily until deescalated as clinically warranted

The intensity of the above observations will be increased as clinically indicated by adverse interim events

B) Adverse effect will be assessed 6 hours post-delivery (e.g., hypertension, fever, vomiting, shivering, epigastric discomfort/ fullness, diarrhoea, headache, chest pain, palpitation, shortness of breath)

C) Full blood count post-delivery (at about 24 hours)

### 3.10 Key Milestones of Study Activity

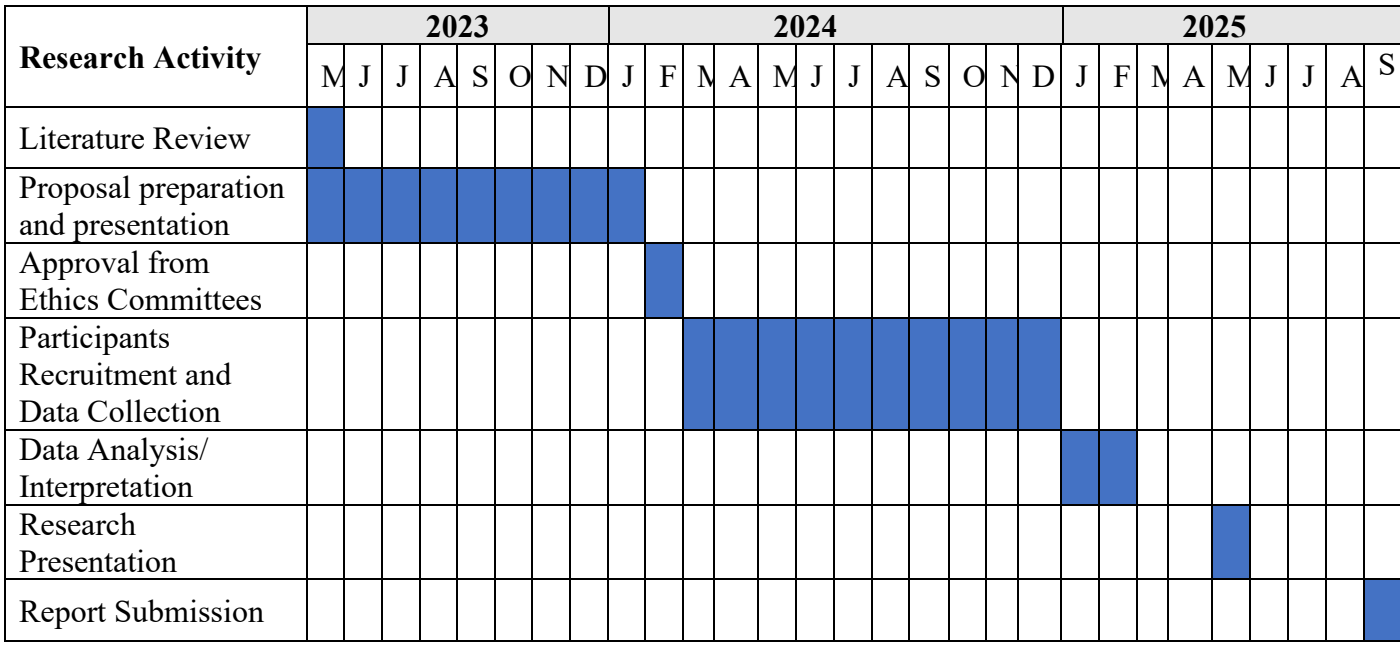
Data collection - March 2024 to Dec 2024

Data analysis - Jan-Feb 2025

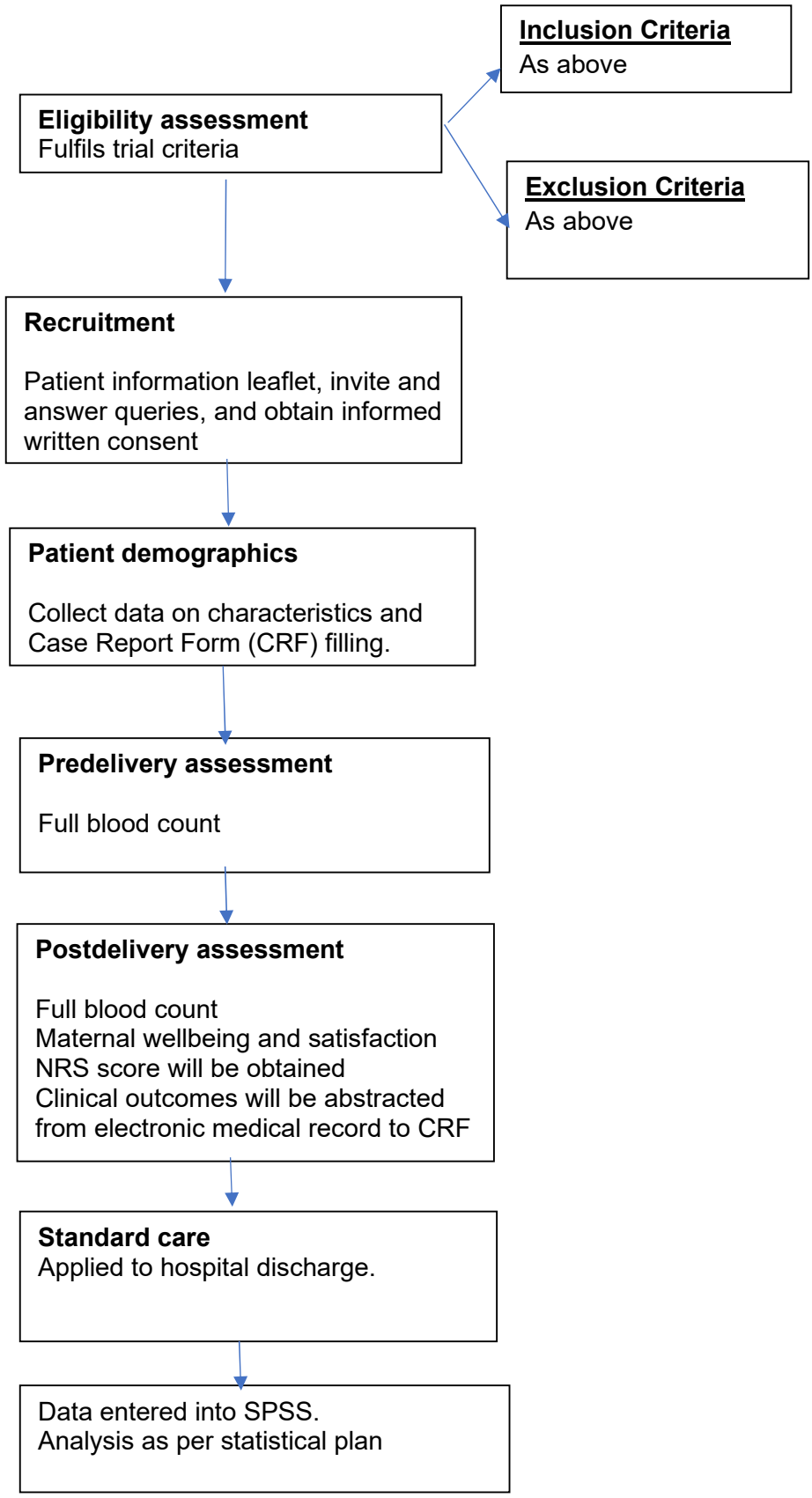
Research presentation - May 2025

Report submission - Sep 2025

### 3.11 Gantt Chart of Study Activity



## CHAPTER 4 : STUDY FLOW CHART



**APPENDIX A**

**ELIGIBILITY ASSESSMENT FORM**

**Inclusion criteria (must fulfil all, tick circles fulfilled):**

- Women expecting a vaginal delivery
- Age 18-45 years
- Term gestation (>37weeks)
- Single fetus
- Cephalic presentation
- Parity <5
- **Final inclusion for randomization: have achieved vaginal delivery**

**Exclusion criteria (must not have any, tick relevant circle/s to exclude):**

- Contraindication or allergy to
    - Oxytocin
    - Misoprostol
    - ergometrine
- Known
    - Hypertension
    - Cardiovascular disorder
    - Hepatic disorder
    - Haematologic disorder
- Cannot communicate in Malay or English

    - Fulfils criteria: Agree / Decline participation (circle as appropriate)

**APPENDIX B**

**CASE REPORT FORM**

STUDY NUMBER

Date of recruitment: __ / __ / __ (dd/ mm/ yy)

EDD: __ / __ / __ (dd/ mm/ yy)

**Patient characteristics**

D.O.B: : __ / __ / __ (dd/ mm/ yy)

Gravida: _____ Para: _____

Gestational age: _____

Latest recorded Weight (predelivery): _____ kg

Height: _____ cm

**Education level:**

Up to Secondary

Diploma

Degree

Masters

PhD

**Occupation:**

Employed

Self employed

Student

Housewife

Other: _____

**Ethnicity**:

Malay

Chinese

Indian

Other: _____

**Labour Onset Spontaneous / Induced / PROM**

**Oxytocin in labour** Yes / No

**Epidural analgesia** Yes / No

**Mode of delivery:**

SVD

Vacuum

Forceps

**Date and Time of Delivery: _____/_____/_____ (dd/mm/yy) ____:____(mm:hr)**

**To be assessed within 24 hours of delivery (from participant)**

1. Rate your current general well being

   Circle your score below (higher score, greater satisfaction)

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

0- totally dissatisfied 10-totally satisfied
(To be assessed within 24 hours of delivery)

2. Rate your experience of the allocated intervention to reduce blood loss at delivery

   Circle your score below (higher score, greater satisfaction)

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

0- totally dissatisfied 10-totally satisfied

3. I would recommend my intervention to a friend (circle one response)

   a) Strongly disagree
   b) Disagree
   c) Neither agrees nor disagrees
   d) Agree
   e) Strongly agree

4. First satisfactory breastfeeding

   Date and Time: _____/_____/_____ (dd/mm/yy) ____:____(mm:hr)

5. Adverse effects (cumulative, ascertained at 6 hours after delivery)

| | | |
|---|---|---|
| a. | hypertension | No / Yes (from EMR) |
| b. | fever | No / Yes (from EMR) |
| c. | vomiting | No / Yes |
| d. | shivering | No / Yes |
| e. | epigastric discomfort or fullness | No / Yes |
| f. | diarrhoea | No / Yes |
| g. | headache | No / Yes |
| h. | chest pain | No / Yes |
| i. | palpitation | No / Yes |
| j. | shortness of breath | No / Yes |

**Primary Outcomes**

At 1 hour post delivery

Blood pressure: Systolic_____mmHg Diastolic_____mmHg

Temperature: ____.___ $^0$C

**Secondary Outcomes**

1. Predelivery haematocrit: _____ Date: _____/_____/_____ (dd/mm/yy)
2. Postdelivery haematocrit: : _____ Date: _____/_____/_____ (dd/mm/yy)
3. Use of additional haemostatic intervention (circle as many as applied)
    a. Uterotonic (birth to hospital discharge)
        i. Oxytocin infusion
        ii. Syntometrine
        iii. Carboprost
        iv. Ergometrine
        v. Misoprostol
        vi. Gemeprost
        vii. Other_____
    b. Surgical (birth to hospital discharge)
        i. EUA
        ii. Manual removal of placenta/tissue
        iii. Balloon tamponade
        iv. Laparotomy
        v. Uterine / Internal iliac artery ligation
        vi. Compressive suture
        vii. Other_____
4. Blood transfusion No / Yes _____ Units (birth to hospital discharge)

5. HDU / ICU (birth to hospital discharge)

6. Shock No / Yes (birth to hospital discharge)
    a. Hypotension (< 90/60 mmHg)
    b. Tachycardia (≥ 120 bpm)
    c. Tachypnoea (> 20 bpm)
    d. Confusion
    e. Peripheral shut down (cold, clammy, mottled skin)
    f. Oliguria (< 20 ml/hr)
    g. Metabolic acidosis
    h. Hyperlactatemia
7. Coagulopathy No / Yes INR_____APTT_____Fibrinogen_____ (birth to hospital discharge)
8. Hysterectomy No / Yes (birth to hospital discharge)
9. Organ dysfunction (birth to hospital discharge)
    a. Renal
    b. Pulmonary
    c. Liver
    d. Other_____
10. Maternal death No / Yes (birth to hospital discharge)
11. Blood pressure
    a. Highest systolic BP recorded (birth to hospital discharge)

        _____mmHg
    b. Highest diastolic BP recorded (birth to hospital discharge)

        _____mmHg

c. Lowest systolic BP recorded (birth to hospital discharge)

_____mmHg

d. Lowest diastolic BP recorded (birth to hospital discharge)

_____mmHg

12. Highest temperature recorded (birth to hospital discharge) _____.___ $^{0}$C

13. Vaginal bleeding as documented (after EBL assessment to hospital discharge)

a. Normal lochia ☐

b. Heavy lochia ☐

c. Haemorrhage _____ ml ☐

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