UNIVERSITY OF MALAYA

The Leader in Research & Innovation

Version 1 **28-09-2018**

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

TITLE

Outpatient vs inpatient Foley catheter induction of labour in multiparous women: A randomised trial

CANDIDATE:
DR TAN YI PIN
MGG160004

SUPERVISOR:

PROFESSOR DR. TAN PENG CHIONG
PROFESSOR DR. SITI ZAWIAH OMAR

TABLE OF CONTENTS

TITLE

Outpatient vs inpatient Foley catheter induction of labour in multiparous women: A randomised trial

INTRODUCTION AND LITERATURE REVIEW

According to data from National Health Service Maternal Statistic published on 9th November 2017, there have been increases in the induction of labour in United Kingdom from 20.3 per cent to 29.4 per cent in the period 2006-07 to 2016-17.[1] Data from the ARRIVE trial[2] shows that induction of labour at 39 weeks in nulliparous reduces Caesarean delivery rate and neonatal respiratory support, findings which could drive the labour induction rate even higher.

Induction of labour may or may not require cervical ripening. According to NHS, about 30% of induction of labour commenced by amniotomy and oxytocin augmentation without the need for cervical ripening.[1] Whereas the remaining 70% requires mechanical or pharmacological methods to ripen the cervix.[1] The Cochrane review suggests that mechanical methods have equivalent clinical effectiveness and have lower rates of hyperstimulation with fetal heart rate (FHR) changes compared to prostaglandin.[3]

The course of labour by prostaglandin induction is less predictable. Some patient would progress into active phase of labour after prostaglandin induction, as shown in PROBAAT trials[4] where less oxytocin augmentation required in prostaglandin group compared to foley group. On the other hand, Foley induction ripens the cervix and rarely causes progression to spontaneous labour without amniotomy and oxytocin augmentation.[5] This allows the induction process to be more controlled. Hence it is practical for foley induction to be used as outpatient basis. The induction process can be started in the evening ay 8pm and the patient can come back the next day (after 12 hours)[6] at a more convenient time whereby the cervix would have ripened and amniotomy/oxytocin can be commenced to allow progression into labour.

Foley catheter rarely causes uterine contraction, pain/discomfort, vaginal bleeding, non-reassuring fetal heart rate, uterine tachysystole, uterine rupture and intrauterine infection.[7] In a systemic review, the estimated prevalence of the analysed adverse events was between 0 to 0.26%.[7] This also makes it an ideal method of cervical ripening for outpatient basis. World Health Organization also recommends the use of a foley catheter as a mechanical method for induction of labour due to its safety and high efficacy.[8]

Foley catheter used for cervical ripening in the outpatient and the inpatient setting resulted in similar mean change in Bishop score and induction time but hospitalization time is reduced by 9.6 hours in the outpatient group.[9]

Outpatient induction of labour allow patient to be go back home after introduction of induction agent. It has been shown to result in higher level of maternal satisfaction with the care during the induction period.[10]

Study by Levine et al, showed the mean duration from induction to delivery interval for multiparous women with foley catheter is about 14.8hours .[11] We proposed cervical ripening process to be started in the evening around 8pm and this may results in delivery during the working hours which is from 8am to 6pm, where most of the health care resources will be optimal. Data from Stephansson et al, showed that infant born at night may be at increased risk of early neonatal death.[12] Data from Moaddab et al, also showed that a dramatic increase in U.S. maternal mortality ratio on weekends, despite a likely systematic bias toward admission and delivery of more complex patients on weekdays. A similar phenomenon was seen for stillbirths.[13]

We hypothesise that induction of labour which started in the evening will result in higher patient satisfaction and permit a larger proportion of delivery at usual working hours (8 am to 6 pm).

OBJECTIVE OF STUDY

The purpose of this study is to look at maternal satisfaction with outpatient Foley catheter induction of labor as compared to inpatient setting and to achieve more delivery during normal working hours (8am to 6pm)

RESEARCH HYPOTHESIS

Outpatient induction of labour with Foley catheter in a parous woman with an unfavourable cervix will be more acceptable and convenience. This may improve the maternal satisfaction with the induction process. We believed that it will also shortens the total duration of hospital stay and may results in more delivery during the normal working hours (8am to 5pm)

ENDPOINTS

Primary endpoint

1. Maternal satisfaction with their care since allocation to the intervention until removal of catheter
2. Delivery during “working hours” (8am to 5pm)

Secondary endpoint

Maternal outcomes

1. Intervention to delivery interval
2. Membrane rupture to delivery interval
3. Mechanism of membrane rupture
4. Oxytocin augmentation
5. Use of additional method(s) for cervical ripening
6. Use of regional analgesia in labour
7. Mode of delivery
8. Estimated blood loss
9. Fever single or more readings of temperature ≥38^{o}C (intrapartum and day 1 postpartum), diagnosis of chorioamnionitis or endometritis
10. Duration of hospital stay
11. Date and time of catheter evacuated/expulsed

Neonatal outcomes

1. Apgar score at 1 and 5minutes
2. Arterial cord pH
3. Birth weight
4. Neonatal admission

METHODOLOGY

Study design
Randomised trial

Population of Study
Multiparous women (with 1/more delivery of neonate more than 500gram) with unfavourable cervix undergoing induction of labour at term in University Malaya Medical Centre, Kuala Lumpur

Inclusion criteria
Aged 18 years and above
Gestational age of ≥ 37 weeks at enrolment
Scheduled induction of labour
Viable pregnancy
Cephalic presentation
Singleton pregnancy
Unfavourable cervix (Bishop Score ≤ 5)
Intact membranes
Reassuring pre induction fetal cardiotocography (CTG)

Exclusion criteria
Allergic to latex
Nulliparous
Previous uterine scar (caesarean/myomectomy)

METHODS

All multiparous women planned for induction of labour by the care provider will be assessed for eligibility and will be counseled regarding this study in the clinic setting. Informed consent will be obtained if the women agreed to participate and patient information sheet will be handled to them. After obtaining informed consent, a vaginal examination will be done to assess bishop score in the clinic setting within 10 days prior to the date of induction. Any women with favourable bishop score will be excluded from the study.

Multiparous women who consented for this study will present themselves to labor room at 8pm on the schedule date of induction for further assessment. Pre-induction fetal cardiotocography (CTG) and assessment of Bishop Score will be done in the labour room. If the CTG and Bishop Score are not suitable, participants will be excluded from the study. Those with favourable Bishop score will be asked to come back the following day for artificial rupture of membrane and oxytocin commencement.

Women will be positioned in the dorsal lithotomy position. A Foley catheter size 16F is introduced through outer cervical canal using either digital or speculum method (on discretion of introducer). Once the tip of the catheter passed the internal os, the catheter will be inflated with 60mL of water and then retracted so that the balloon rested on the cervical os and the external end of the Foley catheter will be taped without tension to the medial aspect of the women's thigh. Fetal monitoring will be performed immediately after inflation of the balloon catheter.

Randomisation will only be carried out once the catheter is in-situ and post foley catheter insertion CTG is normal. Randomisation is by the opening of sealed opaque and numbered envelope with lowest available envelope assigned in strict order. Randomisation will be done using a random number generator at Random.org in random block of 4 or 8 sequence, generated by investigator who is not involved in recruitment. Blinding is not possible due to the nature of the intervention.

For outpatient group, patient will be given a written document with all the information that should bring them back to the hospital, such as: leaking of amniotic fluid or per vaginal bleeding; pain or severe discomfort; decreased fetal movements; painful contractility (>2contractions/10 min) and fever ($T > 38^0C$). They will be asked to come back the next day morning at 8am for removal of foley catheter.

Patient in inpatient group were monitored and oriented in accordance to the Department's protocol. Foley catheter will be removed if spontaneous ruptured of membrane occurs, suspected fetal distress from CTG and or if it still present 12 hours after placement.

Failed induction is diagnosed when the Bishop score ≤ 5 after removal of catheter. If failed induction occurs, patient will be assessed and counseled again by care provider for medical induction of labor or caesarean section.

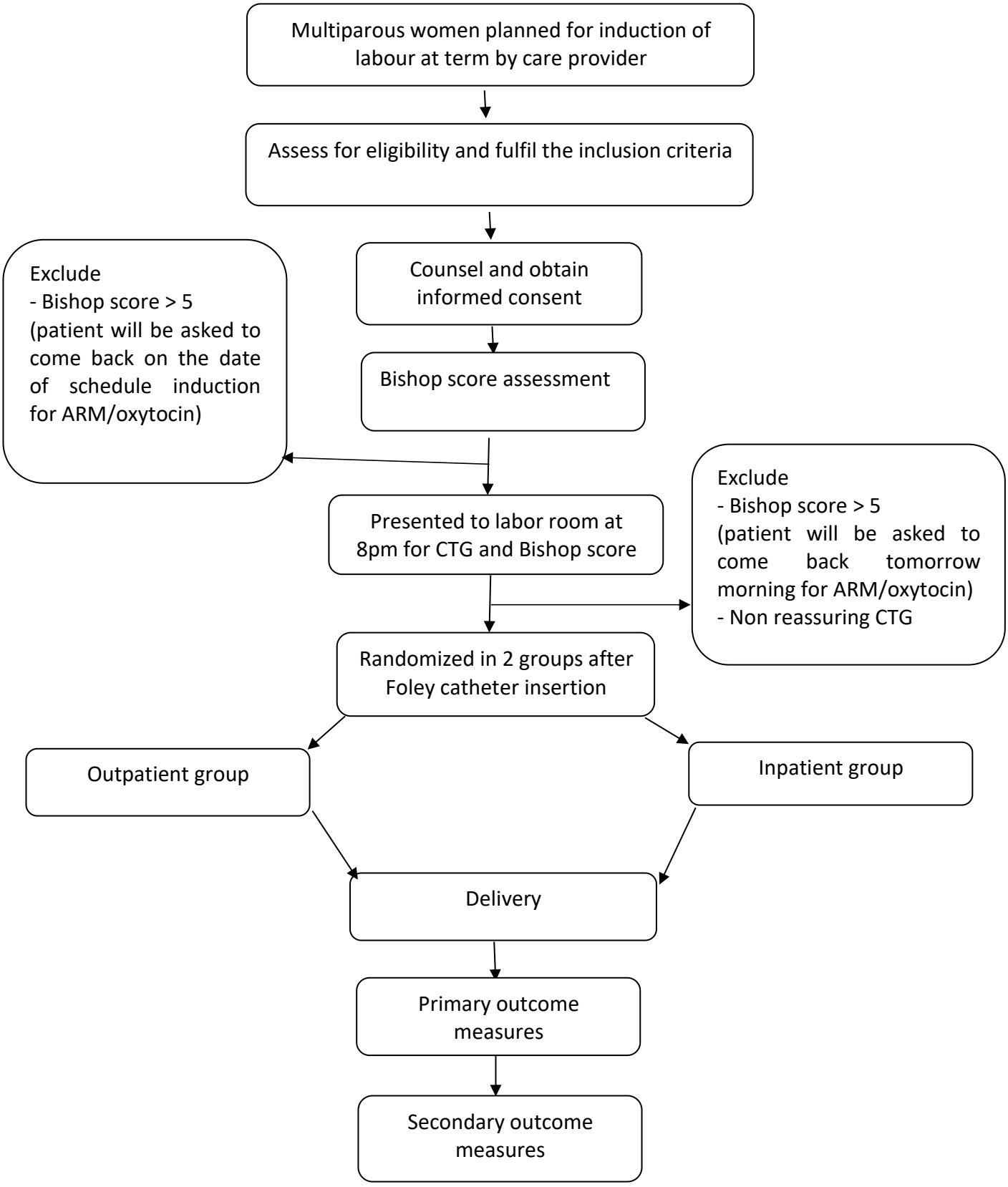
After removal of Foley catheter, amniotomy and oxytocin augmentation will be started and managed according to the care provider practice.

Standard care will be provided to all women in the trial for their labour induction (if needed) and their labour, delivery and post-delivery care. Care providers have full discretion in deciding care in the patients' best interest at all times.

Maternal satisfaction scores for induction process will be assessed after delivery using the visual numerical rating scale and scored from 0-10

Data will be collected as per case report form.

STUDY PROTOCOL FLOW CHART



CASE REPORT FORM

Study Number

Patient's Sticker

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

Patient characteristics
Age : _____
Gravida : _____ Para : _____ Abortion : _____
Gestational age : _____

Latest recorded weight : _____ kg
Height : _____ cm

Education level :
- Up to primary
- Secondary
- Diploma
- Degree
- Masters
- PhD

Occupation :
- Employed
- Self employed
- Student
- Housewife
- Other : _____

Ethnicity :
- Malay
- Chinese
- Indian
- Other : _____

Indication/s for IOL : _____

Pre induction Bishop Score : _____

Score	0	1	2	3
Dilation	Closed	1-2 cm	3-4 cm	≥ 5 cm
Length	> 4 cm	3-4 cm	1-2 cm	O cm
Consistency	Firm	Medium	Soft	
Position	Posterior	Mid	Anterior	
Station	≤-3 cm	-2 cm	-1,-0 cm	≥ 1 cm

Primary Outcome

1. Maternal satisfaction with their care from allocation to intervention until birth (Assessed within 24hours of delivery). Circle the score below:

0	1	2	3	4	5	6	7	8	9	10

Very dissatisfied 

Very satisfied 

2. Time of insertion
   Date : __ / __ / __ (dd/ mm/ yy)
   Time of insertion : ___:___(hr:min)
   Time of delivery
   Date : ___/ ___/ ___ (dd/mm/yy)
   Time : ___:___ (hr:min

Secondary Outcome

Maternal outcome

1. Date and Time of catheter evacuated : __ / __ / __ (dd/ mm/ yy)
   : _____:_____ (hr:min)

2. Date and Time of membrane ruptured : __ / __ / __ (dd/ mm/ yy)
   : _____:_____ (hr:min)

3. Mechanism of membrane ruptured :
   _____

4. Outpatient group – presented back earlier than expected :
   Yes Please specify:_____
   No

5. Use of oxytocin for augmentation :
   Yes Please specify time started:_____
   No

6. Use of additional prostaglandin for cervical?
   Yes Please specify: _____
   No

7. Use of regional analgesia in labour?
   Yes Please specify: _____
   No

8. Mode of Delivery:
   SVD
   Caesarean section. Indication: _____
   Instrumental delivery: Forceps / Vacuum. Indication : _____

9. Estimated blood loss at delivery: _____ ml

10. Temperature: Intrapartum _____ ^{0}C Day 1 Postpartum _____ ^{0}C

11. Total duration of hospital stay : _____(hours)

Neonatal Outcome

1. Apgar Score : _____ 1 mins / _____ 5 mins

2. Arterial Cord pH : _____

3. Birth weight : _____ kg

4. Required neonatal admission :
   Yes
   No

   Place of admission : PNW / SCN / NICU / Others

   Reason for admission : _____

Questionaires to be completed by participant

1) Before reviewing intention to treat (randomization into outpatient vs inpatient group)

   Preference option :

   Outpatient
   Inpatient

2) After delivery

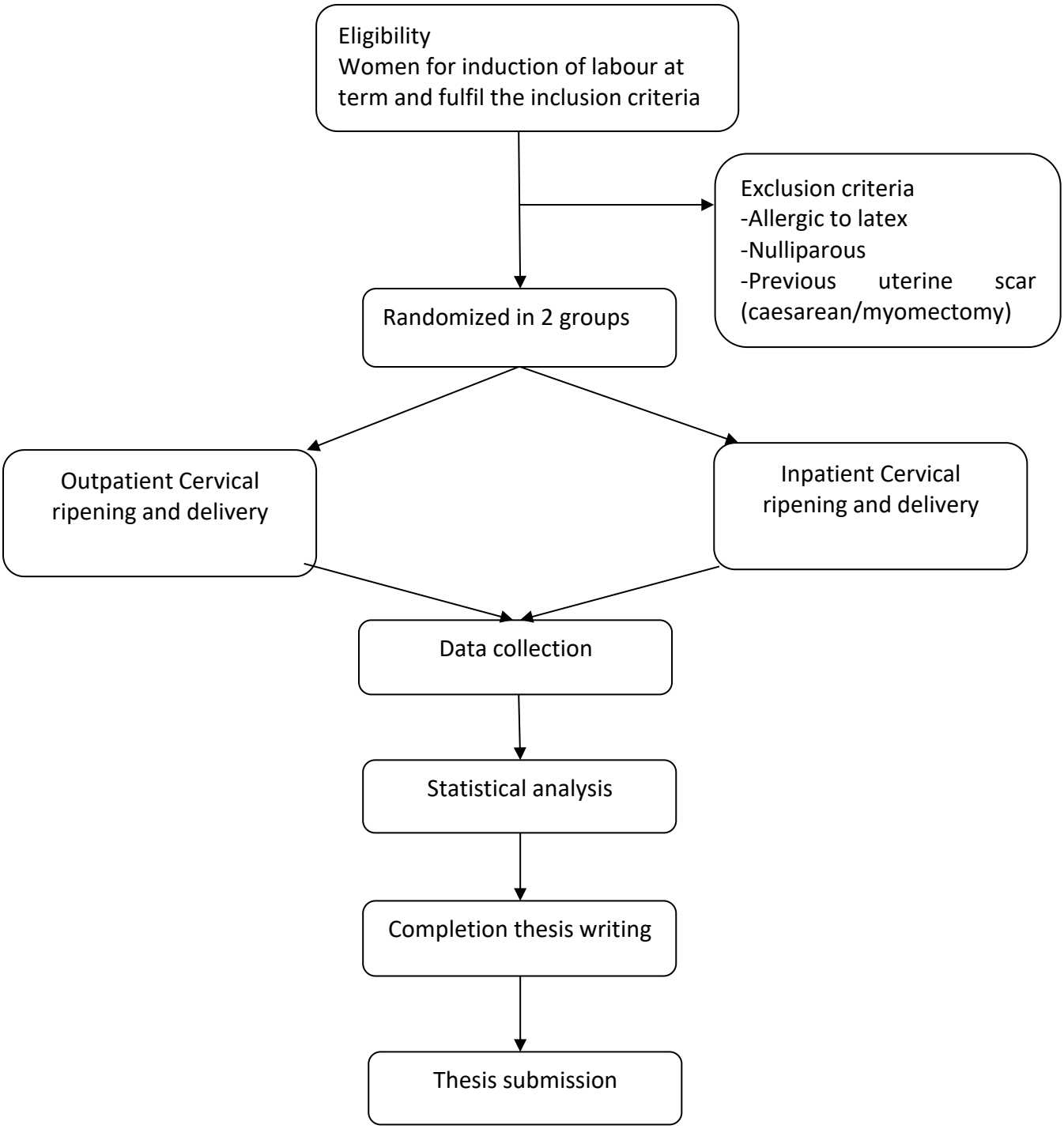
   Would you consider the similar induction process in the next pregnancy if you have been in the same scenario?

   1. Strongly disagree
   2. Disagree
   3. Neither agree nor disagree
   4. Agree
   5. Strongly agree

   Would you recommend this to your friend with the similar scenario like you?

   1. Strongly disagree
   2. Disagree
   3. Neither agree nor disagree
   4. Agree
   5. Strongly agree

STUDY FLOW CHART



ETHICAL CONSIDERATION

This study is submitted to the UMMC Medical Research and Ethics committee, the local institutional review board for approval. Patient will be given an information sheet, have their oral queries addressed and written informed consent obtained to participate in the study.

SAMPLE SIZE CALCULATION

We aim to power our study for 2 primary outcomes, which are delivery during working hours (8am to 5pm) and maternal satisfaction on induction process. PS program version 3.1.2 is used to calculate sample size.

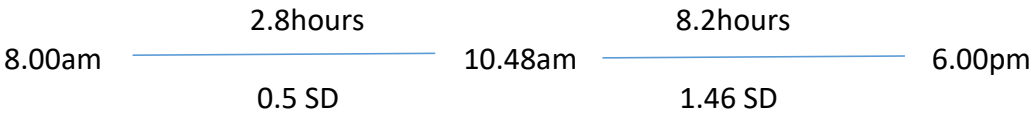
Delivery during working hours (8am to 6pm)

Levine et al, showed that intervention to delivery interval for multipara is 14.8 hours (with interquartile range from 10.1-17.7hours).[11] Using the formula :

IQR/1.35 = SD	IQR: interquartile range
7.6/1.35 = 5.6	SD: standard deviation

Standard deviation is 5.6hours. The intervention to delivery interval for multipara will be 14.8 ± 5.6hours. In this study, once Foley catheter was out whether spontaneous or removed after 12hours, oxytocin augmentation started immediately. This management will be similar to inpatient group of patient in our study. Our study planned to look at delivery during office hours (8am to 6pm). The number of patient expected to deliver during this specified time (8am to 6pm) if we started the induction process at 8pm will be 59.22%. How to arrive at 59.22%?

Induction process starts at 8pm, mean time for delivery will be 10.48hours (14.8 ± 5.6hours).



Assuming normal distribution, patient delivering from 8.00am to 10.48am which is 0.5SD from mean will be 19.15%. Patient delivering from 10.48am to 6.00pm which is 1.46SD from mean will be 36.69%. Total patient delivering during 8.00am to 6.00pm will be 19.15% + 40.07% = 59.22%.

In outpatient group of patient, if foley catheter dislodged at home without any signs of labour, patient will be asked to come back the next day morning at 8am for amniotomy ± oxytocin augmentation. In our local study by Tan et al (2013)[13], about 90% delivers vaginally within 10 hours from amniotomy. If we start amniotomy at 8 am, by between 8 to 6pm same day, about 90% should be delivered vaginally in that 10 hours interval.

To be conservative, assuming that only 80% delivers between 8am to 6pm (10hrs interval) in our outpatient arm and 50% (see calculation above for this) only in the inpatient group delivers vaginally between 8 to 5 pm, then taking alpha 0.05, power 90%, 1 to 1

randomisation ratio and applying chi square test, then 51 women are needed in each arm (total 102), assuming 10% drop out 102/0.9 = 114 total needed.

Mother satisfaction score with induction process

For satisfaction score, assuming we are trying to detect a 1 point difference in the Visual Numerical Rating Scale (scored from 0 to 10) satisfaction score and that the standard deviation of the satisfaction score is 2, then taking alpha 0.05, power 80%, 1 to 1 randomisation ratio and applying Student test, then 64 women are needed in each arm (total 128). Often the distribution of the satisfaction score is not normal and the Mann Whitney U test may have to be applied instead of the Student test, it is customarily to increase the sample size by 10% to take that into account; so (128/0.9) 143 is needed. Factoring in a 10% drop out rate, then (143/0.9) a total of 159 needed.

STATISTICAL ANALYSIS

Data will be entered into SPSS statistical software. Normally distributed continuous data will be analyzed with paired Student's t test. Chi square test will be used for categorical or nominal data and Mann-Whitney U test will be used on non normally distributed or ordinal data.

STUDY DURATION

The delivery rate in University Malaya Medical centre is about 5000 per year. Induction of labour rate approximately is about 30% per year. Out of this about 30% involve parous women.

Assuming that 88% (based on survey) of women will agreed for induction of labour with mechanical method, then 1500 x 0.3 x 0.88 = 396 women might be recruited per year.

We plan to recruit 159 women into this study which should take about 6 months (159/369 x 12 = 5.17)

This study will be conducted from as soon as possible as approved by Ethical Committee Board and should run for 6 months barring unexpected events.

GANNT CHART

Duration	Aug 2018	Aug – Sept 2018	Sept – Nov 2018	Dec 2018 – Octo 2019	Octo 2019 - Dec 2019	Jan 2020
Literature review	✓					
Proposal preparation & presentation	✓	✓				
Ethics review			✓			
Data collection				✓	✓	
Data analysis and writing					✓	✓
Thesis submission						✓

REFERENCES

1. NHS Maternity Statistics, 2016-17: Summary report.
2. Grobman, W. A., et al. (2018). "Labor Induction versus Expectant Management in Low-Risk Nulliparous Women." New England Journal of Medicine **379**(6): 513-523.
3. Jozwiak, M., et al. (2012). "Mechanical methods for induction of labour." Cochrane Database of Systematic Reviews(3).
4. Jozwiak, M., et al. (2011). "Foley catheter versus vaginal prostaglandin E2 gel for induction of labour at term (PROBAAT trial): an open-label, randomised controlled trial." The Lancet **378**(9809): 2095-2103.
5. Sciscione, A. C., et al. (1999). "A prospective, randomized comparison of Foley catheter insertion versus intracervical prostaglandin E2 gel for preinduction cervical ripening." American journal of obstetrics and gynecology **180**(1): 55-59.
6. Aduloju, O. P., et al. (2016). "Combined Foley's catheter with vaginal misoprostol for pre-induction cervical ripening: A randomised controlled trial." Australian and New Zealand Journal of Obstetrics and Gynaecology **56**(6): 578-584.
7. Diederen, M., et al. (2018). "Safety of the balloon catheter for cervical ripening in outpatient care: complications during the period from insertion to expulsion of a balloon catheter in the process of labour induction: a systematic review." BJOG: An International Journal of Obstetrics & Gynaecology **125**(9): 1086-1095.
8. Organization, W. H. (2011). "WHO recommendations for induction of labour: evidence base."
9. Sciscione, A. C., et al. (2001). "Transcervical Foley catheter for preinduction cervical ripening in an outpatient versus inpatient setting." Obstetrics & Gynecology **98**(5): 751-756.
10. Biem, S. R., et al. (2003). "A randomized controlled trial of outpatient versus inpatient labour induction with vaginal controlled-release prostaglandin-E2: effectiveness and satisfaction." Journal of Obstetrics and Gynaecology Canada **25**(1): 23-31.
11. Levine, L. D., et al. (2016). "Mechanical and pharmacologic methods of labor induction: a randomized controlled trial." Obstetrics and gynecology **128**(6): 135
12. Stephansson, O., et al. (2003). "Time of birth and risk of intrapartum and early neonatal death." Epidemiology: 218-222.
13. Moaddab, A., et al. (2018). "Maternal and Fetal Death on Weekends." American journal of perinatology
14. Tan, P. C., et al. (2013). "Immediate compared with delayed oxytocin after amniotomy labor induction in parous women: a randomized controlled trial." Obstetrics & Gynecology **121**(2): 253-259.
15. Farmer, K. C., et al. (1996). "A cost-minimization analysis of intracervical prostaglandin E2 for cervical ripening in an outpatient versus inpatient setting." Clinical therapeutics **18**(4): 747-756.
16. Sciscione, A. C., et al. (2014). "The timing of adverse events with Foley catheter preinduction cervical ripening; implications for outpatient use." American journal of perinatology **31**(09): 781-786.
17. Kelly, A. J., et al. (2009). "Outpatient versus inpatient induction of labour for improving birth outcomes." The Cochrane database of systematic reviews(2): CD007372.
18. Amorosa, J. M. and J. L. Stone (2015). Outpatient cervical ripening. Seminars in perinatology, Elsevier.
19. Schmitz, T., et al. (2014). "Outpatient cervical ripening by nitric oxide donors for prolonged pregnancy: a randomized controlled trial." Obstetrics & Gynecology **124**(6): 1089-1097.
20. Policiano, C., et al. (2017). "Outpatient versus inpatient cervix priming with Foley catheter: A randomized trial." European Journal of Obstetrics & Gynecology and Reproductive Biology **210**: 1-6.
21. Laughon, S. K., et al. (2012). "Induction of labor in a contemporary obstetric cohort." American journal of obstetrics and gynecology **206**(6): 486. e481-486. e489.
22. Policiano, C., et al. (2017). "Efficacy and safety of foley catheter balloon for cervix priming in term pregnancy." Acta medica portuguesa **30**(4): 281-284.
23. Gibson, K. S., et al. (2013). "Inner thigh taping vs traction for cervical ripening with a Foley catheter: a randomized controlled trial." American journal of obstetrics and gynecology **209**(3): 272. e271-272. e277.
24. Sanu, O. (2015). "Outpatient cervical ripening by nitric oxide donors for prolonged pregnancy: a randomized controlled trial." Obstetrics & Gynecology **125**(3): 741-742.