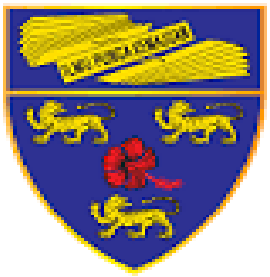

UNIVERSITY OF MALAYA

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RESEARCH PROPOSAL FOR MASTER OF MEDICINE

(OBSTETRICS AND GYNAECOLOGY)

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

UNIVERSITY MALAYA

TITLE

RANDOMISED CONTROLLED TRIAL OF 4 HOURLY VERSUS 8 HOURLY VAGINAL EXAMINATION INTERVAL AFTER AMNIOTOMY AND CERVICAL RIPENING WITH FOLEYS CATHETER IN NULLIPARAS

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1. INTRODUCTION AND LITERATURE REVIEW

Induction of labor (IOL) are defined as process to artificially stimulate uterine contraction to initiate labor. In recent years, the rate of IOL have rise steadily; as many as one in four patient delivered following induction of labor[1]. The current rate of IOL have been supported with many datas which exhibited reduced perinatal morbidity and mortality without affecting maternal outcomes.[2,3,4]

Induction of labor can be performed medically or mechanically. In recent years, the use of mechanical method of induction via foley's catheter have regained it's popularity as many literatures exhibited that mechanical IOL produced comparable results to pharmacological methods of induction of labour without increasing rate of cesarean section and uterine hyper stimulation[5].

Furthermore, early amniotomy and oxytocin infusion preceding expulsion of foley's catheter has been employed as one of the strategies to hasten the labour progress.[6,7,8]

Following IOL patient will undergo labour process. In parturing mother, it is necessary for clinician to monitor labour progress. Labour progress can be monitored via observation and clinical examination. However, the single most effective way of monitoring labour progress are via vaginal examination

WHO advocates routine 4 hourly vaginal examination to assess labour progress[9]. It was tailored loosely based on Friedman work[10]. However, re-examination of Friedman curves on labour progress among current demographic nulliparous have changes; recent evidence exhibited that on average from cervical dilation from 3cm to full dilation of cervix time interval taken for delivery was 5.5 hours, which is much slower in comparison to Friedman work which is around 2.5 hours[11]. The re-examination also has exhibited that median duration of labour from admission to 10 cm of cervical dilation was 7.3 hours (10th and 90th percentiles: 3.3 and 13.7 hours, respectively) [11]

In keeping of recent evident, whereby median delivery time are only anticipated after 7.3 hours in labour, there are question on relevance of routine 4 hourly vaginal examination for patient undergoing IOL with foley's catheter as no intervention can be performed since early amniotomy and oxytocin induction has been initiated early following removal of foley's catheter

Furthermore, frequent vagina examination have been shown to cause discomfort, pain, embarrassment and discomfort among pasturing mother, along with increased risk of infection with no effect on time interval from latent phase of labour to delivery[12-21]

Hypothetically, postulation can be made that protracted interval in between each routine vaginal examination might be beneficial in improving maternal satisfaction and with comparable amniotomy to delivery interval versus standard 4 hourly vaginal examination and in between the interval, vaginal examination should only be reserved for abnormal fetal heart rate pattern, maternal complain of bearing down, fully dilated cervical os with imminent delivery or application fetal scalp electrode for fetal heart monitoring

To further examine the effect of the above-mentioned hypothesis on maternal satisfaction to the fullest, nulliparous women are selected as they have never undergone labour process previously, thus leading to no prejudices on their judgement on their labour experience

2. OBJECTIVE OF STUDY

To show that 8-hourly vaginal examination interval in nulliparas after cervical ripening with Foleys catheter and amniotomy will improve maternal satisfaction and achieve comparable amniotomy to delivery interval versus 4-hourly vaginal examination

3. RESEARCH HYPOTHESIS

We hypothesize that:

1) Eight hourly vaginal examination in nulliparous women after amniotomy and cervical ripening with foleys catheter will result in higher maternal satisfaction and comparable amniotomy to delivery interval versus 4-hourly vaginal examination

OUTCOMES

3.1.1 Primary outcome

1. Maternal satisfaction of labour care measured using a Visual Numerical Rating Score (VNRS) from 0-10, assessed soon after delivery
2. Duration of active labour, defined as amniotomy to delivery interval is assessed from hospital records after hospital discharge

3.1.2 Secondary outcomes

Maternal outcome

1. Mode of delivery
    i. Vaginal delivery and it's rate
    ii. Vaginal assisted delivery and it's rate
    iii. Caesarean section and it's rate
2. Viscera injury
    i. Bowel
    ii. Bladder
    iii. Ureter
3. Hysterectomy
4. Need for operative pelvic floor repair
5. Oxytocin induction/augmentation in labour
6. Maternal infection which is defined from as single temperature reading of 38°C or greater
    i. Intrapartum
    ii. Postpartum
7. Analgesic & epidural used in labour
8. Estimated delivery blood loss
    i. Haemorrhage (Blood loss more than 500cc in Vaginal delivery or 1000cc in caesarean section)

9. Uterine hyperactivity:
    a. Tachysystole (six of more contractions in 10 minutes over two consecutive 10-minute periods)
    b. Hypertonus (sustained contraction 2 min or longer)
    c. hypertonus with fetal heart rate abnormality
10. Uterine rupture/ Scar dehiscence
11. CTG abnormality based on NICE guideline
    a. Suspicious
    b. Pathological
12. Duration of hospital stay
13. Admission into intensive care unit
14. Indication for induction of labour
15. Duration from induction to delivery
16. Cardio-respiratory arrest
17. Post natal depression
18. VTE
    i. Deep Vein Thrombosis
    ii. Pulmonary embolism
    iii. Stroke
19. Maternal death

Neonatal outcomes

1. Apgar score at 1 and 5 minutes
2. Umbilical cord arterial blood pH and base excess
3. Birth weight
4. Birth Trauma
5. Neonatal admission
    a. NICU
    b. Special care nursery
    c. Indication for neonatal admission
6. Hypoxic ischaemic encephalopathy or need for therapeutic hypothermia
7. Meconium aspiration syndrome
8. Need for respiratory support
9. Neonatal infection
10. Neonatal seizures

4. METHODOLOGY

4.1 Study design

Prospective Randomised control trial

4.2 Settings

Labour ward, Women and Child Complex University Malaya Medical Centre

4.3 Duration of study

This study will be conducted for 6 months from 1st May 2021 until 1st December 2021 pending approval of ethic committee

4.4 Study population

Nulliparous women with unfavourable cervix undergoing induction of labour for various reasons at term (more than 37 weeks) at University Malaya Medical Centre, Kuala Lumpur

Inclusion criteria

1. Women who had cervical ripening with Foley catheter only and favourable cervix with cervical dilatation of 3cm or greater (suitable for amniotomy) with contraction < 1:5min
2. Nulliparous
3. No prior pregnancy beyond 20 weeks gestation
4. Age 18 years and above
5. Gestational age of ≥ 37weeks at enrolment scheduled induction of labour
6. Scheduled induction of labour
7. Viable pregnancy
8. Cephalic presentation
9. Singleton pregnancy
10. Reassuring pre induction fetal cardiotocography (CTG)
11. Intact membrane

Exclusion criteria

1. Contraindication to vaginal delivery
2. Known gross fetal anomaly
3. Fetal weight clinically estimated to be ≤ 2 kg & ≥ 4kg and confirmed by ultrasound
4. Previous uterine surgery, ie: myomectomy, hysterotomy and history of iatrogenic uterine perforation

5. SAMPLE SIZE CALCULATION

For maternal satisfaction, assuming a 1-point difference in the visual numerical rating scale and that the standard deviation score is 2, utilising alpha of 0.025 and power of 80%, one to one randomization ratio, Delta 1 and using Student T-test the number required in each arm is 77. If Mann Whitney U test is used for non-normally distributed data (15% sample size increase), total number of each arm becomes 89. Assuming drop out 10%, final number of patients in each arm is 99 with total sample size 198.

We also made literature review on membrane rupture to delivery interval Levy et al. through a prospective RCT of early versus late amniotomy following cervical ripening with a Foley catheter in 178 women, reported that early amniotomy (artificial rupture of membranes immediately after catheter removal/expulsion) resulted in delivery after 9.4H with SD 4.2[7].

Using the above data, with a non-inferiority limit of 2-hour difference in duration of active labour between the 2 groups, we used PS Calculator to calculate the sample size.

Using alpha 0.025, 80% power, standard deviation of 4.2H, 85 women are required per arm (total 170). Assuming 10% dropout rate, 94 women are required in each arm, with total of 188 women in size

6. METHOD

6.1 Patient recruitment

Method

All women who fulfilled the inclusion criteria undergoing induction via Foley catheter insertion are identified by health care providers at delivery suite and antenatal ward. will be assessed for recruitment eligibility by going through their medical records when they attending their scheduled induction of labour in our obstetric unit. Participants who fulfilled the eligible criteria will be provided with patient information sheet and counselled for participation on this study. If women agree to participate, written and informed consent will be taken from participants.

Following removal of foley's catheter, manually or spontaneously, vaginal examination will be performed and participants with cervical dilatation ≥ 3cm will be sent to labour ward for amniotomy. If participants fulfilled final criteria's; (i) cervical os dilatation of ≥ 3cm, (ii) cephalic presentation, (iii) station not higher than -2, (iv) reassuring fetal heart status, randomization will be performed post amniotomy. Titration of intravenous of oxytocin augmentation is at discretion of care provider.

Randomisation will be carried out by opening the lowest numbered seal opaque envelope. Randomization for 1:1 ratio with blocks of 4 and 8 done by an investigator not involved in the recruitment process will be used to generate the randomization code. Participants will be randomized to either intervention group (Group 1) or control group (Group 2).

Participants in intervention group will be subjected to 8 hourly routine vaginal examination while participants in control group will be subjected to standard 4 hourly routine vaginal examination during labour. Participants on both groups will require additional vaginal examination as per standard care in the event of (i) administration of analgesia/epidural, (ii) fully dilated cervical os, or (iii) application of fetal scalp electrode. Labour progress will be documented in partograph. Fetal heart rate and uterine activity will be monitored continuously during participants labour process.

Following delivery, participants will be asked on maternal satisfaction; "Please rate your satisfaction on your allocated care during your labor ". score will be rated by on both group via Visual Numerical Rating Scale (VNRS) with scoring from 0-10. Data will be collected as per case report form. Detail pertaining participant's delivery outcome will be retrieved from medical notes and will be included in case report form

Standard Induction of labour procedure using Foley's Catheter- During the process of induction, CTG pre induction will be done and Foley's catheter size 16F is introduced through outer cervical canal using either digital or speculum method. Once the tip of catheter passed through the internal os, the catheter will be inflated with 60 ml of water and retracted so that the balloon will be rested on cervical os and the external end of the Foley's catheter will be taped without tension to the medial aspect of the women's thigh.

The standard labour room practise in UMMC is during admission of a parturient- the partogram must be started on diagnosis of established labour and relevant findings recorded in a timely fashion. An entry should be made in patient's notes at least every hour by the care staff in additional to partogram and other relevant chartings. Continuous monitoring of electronic fetal heart rate status will be monitored, together with uterine activity. Maternal pulse, respiration will be monitored at least hourly, maternal temperature will be monitored at least 4hourly, bladder catheterisation and urine analysis will have done every 4hours.

Standard oxytocin regime -Oxytocin infusion will be prepared by diluting 10iu of oxytocin into 500ml Hartmann's solution (oxytocin concentration of 20milliunits/ml)

It will be titrated every half an hour based on uterine activity starting at 6ml/hr, doubling up, to the maximal rate of 96 ml/ hr.

The optimal contraction needed are about 3 to 4 moderates to strong contractions in 10 minutes, and when the optimal contraction is obtained, the oxytocin is maintained at the current rate.

6.2 Definition of operational terms[22]

Vaginal examination is performed digitally with a sterile gloved hand. The digital vaginal examination primarily assess how far the uterine cervix has thinned and dilated. The full components of the vaginal examination, as described in detail by Simkin[22]:
The cervix:

- Position of the cervical os (posterior to anterior)
- Consistency of the cervix (from hard to soft, or 'ripe')
- Effacement of the cervix (from thick to thin)
- Dilation of the cervical os (from 0 to 10 centimetres, nominally)

The fetal presenting part:

- Degree of rotation (to the anterior)
- Degree of flexion (from deflexed to flexed)
- Amount of moulding (if cephalic)
- Degree of descent into the maternal pelvis

State of the amnion:

- Intact or not
- Degree of application to the presenting part of the fetus

- Degree of bulging when under pressure from a contraction

State of mother:

- Any obvious contraction of the maternal pelvis

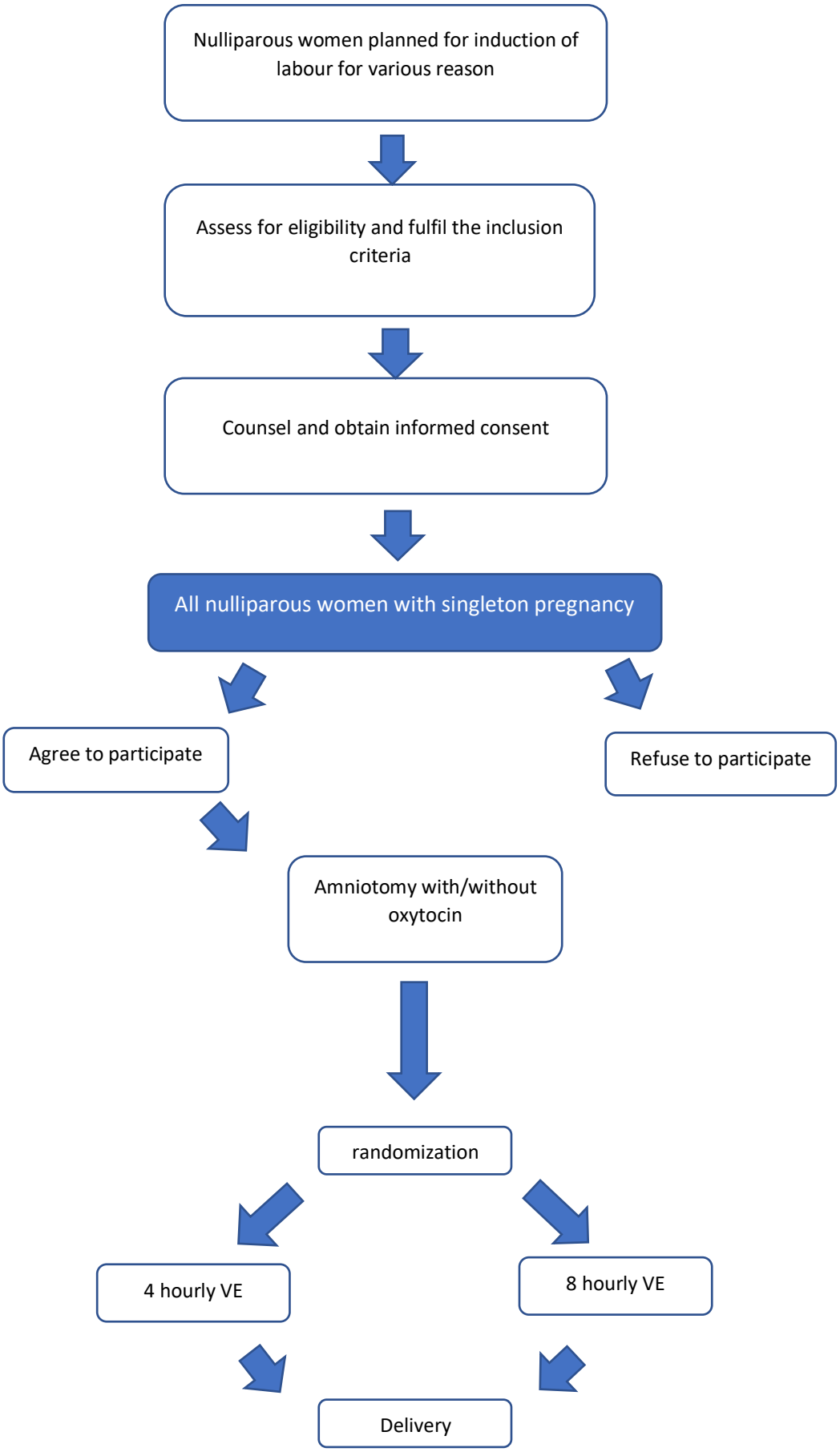
7. STATISTICAL ANALYSIS

Data will be entered into SPSS statistical software. Normally distributed continuous data will be analysed 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. During this trial, an interim analysis will be conducted.

8. ETHICAL CONSIDERATION

This study will be submitted to the UMMC Medical Research and Ethics committee, the local institutional review board for approval. All the participants involved in this study will be reassured about the confidentiality and informed written consent is compulsory. This trial is designed as cross-sectional study. Patient will be given an information sheet, have their oral queries addressed and written informed consent obtained to participate in the study. There is no conflict of interest in this study.

9. STUDY FLOW CHART



ELIGIBILITY SCREENING AND RECRUITMENT FORM
STUDY TITLE: 4 HOURLY VERSUS 8 HOURLY VAGINAL EXAMINATON IN NULLIPAROUS WOMEN

Patient's Sticker

Date: _____/_____/_____
EDD _____/_____/_____ (_____ POA/POG)

Inclusion criteria

- ☐ a) Nulliparous women
- ☐ b) Aged ≥18 years
- ☐ c) Gestational age of > 37 weeks at enrolment of scheduled induction of labour
- ☐ d) Viable pregnancy
- ☐ e) Cephalic presentation
- ☐ f) Singleton pregnancy
- ☐ g) Favourable cervix, (cervical os ≥ 3cm), prior to amniotomy
- ☐ h) post Foley's induction
- ☐ i) Reassuring fetal heart status (CTG)

Exclusion criteria

- ☐ j) Previous uterine incision/ injury (Caesarean delivery, myomectomy, perforation)
- ☐ k) Gross fetal anomaly
- ☐ l) Contraindication for vaginal birth
- ☐ m) Estimated fetal weight < 2kg > 4 kg before induction
- ☐ n) multipara

Not Eligible ☐ **Eligible but declined** ☐ **Eligible and consented** ☐

CASE REPORT FORM

Study Number

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

Patient's Sticker

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 : _____

Primary Outcome

1. Time of amniotomy

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

Time of amniotomy : ___:___(hr:min)

2. Time of oxytocin

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

Time of oxytocin : ___:___(hr:min)

3. Time of delivery

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

Time of delivery : ___:___(hr:min)

4. Maternal satisfaction

Please rate your satisfaction on your allotted care during your labor

0	1	2	3	4	5	6	7	8	9	10

Complete dissatisfied

Completely satisfied

Secondary Outcome

5. Duration from induction to delivery_____
6. Mode of Delivery:
    a. □ SVD
    b. □ Caesarean section. Indication: _____
    c. □ Instrumental delivery: Forceps / Vacuum. Indication : _____
7. Uterine Hyperstimulation □ yes □ no
    a. Tachysystole (six of more contractions in 10 minutes over two consecutive 10-minute periods) □ yes □ no
    b. Hypertonus (sustained contraction 2 min or longer) □ yes □ no
    c. hypertonus with fetal heart rate abnormality □ yes □ no
8. Uterine rupture/ Scar dehiscence □ yes □ no
9. CTG abnormality based on NICE guideline □ yes □ no
    a. Suspicious □ yes □ no
    b. Pathological □ yes □ no
10. Hysterectomy? □ yes □ no
11. Viscera injury? □ yes □ no
    a. □ bladder □ bowel □ Ureter
12. ICU admission? □ yes □ No
13. Duration of hospital stay_____
14. Maternal infection: Intrapartum _____ ^{0}C Postpartum _____ ^{0}C
15. Analgesic use in labour ? □ Yes □ No
    a. If yes, please specify: _____.
16. Estimated blood loss at delivery: _____ ml
17. Degree of perineal tear
    a. □ 1st degree □ 2nd degree □ 3rd degree □ 4th degree
    b. Requiring EUA? □ Yes Please specify _____ □ No
18. VTE
    a. Deep Vein Thrombosis □ Yes □ No
    b. Pulmonary embolism □ Yes □ No
    c. Stroke □ Yes □ No
19. Cardio-respiratory arrest □ Yes □ No
20. Post natal depression □ Yes □ No
21. Maternal death □ Yes □ No.
    a. If yes, specify cause of death_____

Neonatal Outcome

1. Apgar Score : _____ 1 mins / _____ 5 mins
2. Arterial Cord pH : _____ Base Excess : _____
3. Birth weight : _____ kg
4. Required neonatal admission : ☐ Yes ☐ No
    a. Place of admission : SCN / NICU / Others
    b. Indication for admission _____
5. Hypoxic ischaemic encephalopathy or need for therapeutic hypothermia ☐ Yes ☐ No
6. Meconium aspiration syndrome ☐ Yes ☐ No
7. Need for respiratory support ☐ Yes ☐ No
8. Neonatal infection ☐ Yes ☐ No
9. Neonatal seizures ☐ Yes ☐ No

11.0 GANTT CHART

	2021										
	Feb 2021	Mac 2021	April 2021	May 2021	June 2021	July 2021	Aug 2021	Sept 2021	Oct 2021	Nov 2021	Dec 2021
Research proposal and preparation											
Presentation to department											
Presentation to ethics committee and approval											
Patient recruitment and data collection											
Data entry											
Data analysis											
Thesis writing											
Thesis submission											

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