BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-033844
Article Type:	Protocol
Date Submitted by the Author:	24-Aug-2019
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Keywords:	Breathing exercises, Reflexology, Massage, Primigravidae, Labour pain, Stress hormones

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Effectiveness of Breathing Exercises, Foot Reflexology and Back Massage (BRM) on Labour Pain, Anxiety, Duration, Satisfaction, Stress Hormones and New-born Outcomes among Primigravidae during the First Stage of Labour in Saudi Arabia: A Study Protocol for a Randomised Controlled Trial

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ABSTRACT

Introduction Labour pain is among the severest pains primigravidae may experience during pregnancy. Failure to address labour pain and anxiety may lead to abnormal labour. Despite the many complementary non-pharmacological approaches, the quality of evidence is low, and best approaches are not established. This study protocol describes a proposed investigation of the effects of a combination of breathing exercises, foot reflexology and back massage (BRM) on the labour experiences of primigravidae.

Methods and analysis This randomised controlled trial will involve an intervention group receiving BRM and a control group receiving standard labour care. Primigravidae of 26–34 weeks of gestation without chronic diseases or pregnancy-related complications will be recruited from antenatal clinics. Eligible and consenting patients will be randomly allocated to the intervention or the control group stratified by intramuscular pethidine use. The BRM intervention will be delivered by trained masseuses. The primary outcomes of labour pain and anxiety will be measured during and after uterine contractions at baseline (cervical dilatation 6 cm) and post-BRM hourly for two hours. The secondary outcomes include maternal stress hormone (adrenocorticotropic hormone, cortisol and oxytocin) levels, maternal vital signs, labour duration, maternal satisfaction, foetal heart rate and Apgar scores. The sample size is estimated based on the between-group difference of 0.6 in anxiety scores, 95% power and 5% α error, which yields a required sample size of 154 (77 in each group) accounting for a 20% attrition rate. The between- and within-group outcome measures will be examined with mixed-effects regression models, time series analyses and paired t-test or equivalent non-parametric tests, respectively.

Ethics and dissemination Ethical approval was obtained from the Ethical Committee for Research Involving Human Subjects of the Ministry of Health in the Saudi Arabia (H-02-

K-076-0319-109) on 14 April 2019. Written informed consent will be obtained from all the participants.

Trial registration number and date ISRCTN87414969, registered 3 May 2019

Keywords Breathing exercises, Reflexology, Massage, Primigravidae, Labour pain, Stress hormones.

Article Summary

Strengths and Limitations of the Study

- This single-blinded parallel randomised controlled trial will explore the combined effects of breathing exercises, feet reflexology and back massage (BRM) on pain and anxiety relief during labour in healthy primigravidae with singleton foetus.
- The effects of BRM will be examined through the objective physiological outcomes of stress hormone levels between groups before and after the intervention.
- Trained masseuses will deliver BRM to pregnant women.
- The intervention will be applied for one hour and only once during the first stage of labour after cervical dilatation of 6 centimetres.
- Blinding of the primigravidae mothers is not possible, and there may be bias in the self-assessed outcomes.

Word count 4,091 words

INTRODUCTION

Many primigravidae have reported experiencing various levels of pain and high levels of anxiety about the labour process and outcomes. These feelings of pain and anxiety may

occur in the early stages of labour and during labour itself[1–3]. Anxiety extending to fear is a common issue related to labour, especially among primigravidae[4,5]. Other recorded negative perceptions and psychological effects influencing labour experiences include distress and feelings of powerlessness during labour for women and their families[5–7].

When poorly managed, labour pain may lead to severe consequences for women such as prolonged labour[5,8], which may increase the risk of foetal distress, head compressions, intrauterine foetal death, low Apgar scores and physical injuries to neonates[5,9]. Prolong labour results in increased risk of caesarean section, induced labour and assisted delivery using vacuum and forceps[10,11]. Studies have also reported negative mental impacts on women, sometimes to the extent of postnatal post-traumatic anxiety disorder[12,13] and subsequently reduced quality of life[14]. Feelings of anxiety often originate from possible birthing complications about which pregnant women have heard and read[4,5,15,16] and may even result in women refusing normal vaginal delivery and insisting on caesarean sections without medical indications[17]. It, therefore, is important for healthcare professionals to assist and educate all expectant mothers on labour pain management.

Appropriate labour pain management and interventions are important aspects of obstetric care to ensure optimum outcomes for mothers and babies[18]. Pharmacologic interventions used in management of labour pain include systemic sedatives, analgesics and regional anaesthesia[19]. Examples of these analgesics are aerosol and epidural opioids, intramuscular pethidine (IMP) and intravenous sedatives[20,21]. Some of these are expensive and may be associated with adverse effects on mothers, the labour process and neonates [22].

In contrast, most non-pharmacological methods for labour pain management are simple and non-invasive and often are cheaper and safer than pharmacological interventions[23–25]. Studies have found that non-pharmacological approaches, particularly breathing exercises, have positive impacts on relief of labour pain[26–28] and anxiety in pregnant mothers[29–31]. Non-pharmacological approaches areespecially true for Lamaze breathing, deep breathing exercises[26–28,32,33], reflexology[34,35] and massage[36]. Non-pharmacology has been linked to a shorter labour duration[37] and improved new-born outcomes[38]. Our systematic review found that massage is beneficial for relieving labour pain[39] and is associated with greater relaxation, higher alertness levels, improved mood and reduced stress hormone (cortisol) levels and anxiety symptoms[40].

Rationale

It is hypothesised that non-pharmacological approach of labour pain management occurs via the alteration of nociceptive stimuli and modification of the processing of nociceptive input at the central level. With that, there is an overall improved sense of comfort and well-being, ultimately leading to stronger coping capabilities by the mothers in labour [41].

The physiological mechanism of breathing is a protective action as it is a fight-or-flight reflex triggered by the central nervous system. Physiologically, deep abdominal breathing stimulates the parasympathetic nervous system. As a result, the blood circulation in pregnant women will undergo oxygenation, during which it will trigger the release of endorphins which are associated with the decrease in heart rate and promoting the releasing the feelings of calmness. At the same time, endorphins can also suppress the sympathetic system, leading to a decrease in the release of stress hormones such as cortisol [42,43].

As for reflexology, so far there has been no constructive explanation on the underlying mechanism in reducing labour pain [35,37]. However, there are several postulated theories for its mechanism of action. Firstly, the autonomic-somatic integration theory suggests that the pressure applied to the feet during reflexology compresses the receptors in the cells, thus opening up the ionic channels in the plasma membrane and triggering a local action potential to convey messages to the spinal cord and/or brain [44]. The application of alternating pressure to the feet may also produce predictable reflexive actions within the nervous system and activates the parasympathetic nervous system [45].

Another contemporary method explains that reflexology acts through a "sympathetic resonance" manner, in which energy wave between therapist and clients are inter-conducted to achieve homeostatic balance [46]. This may occur through local enzymatic reactions on receptive fields or through an improved blood supply as a result of local skin temperature changes following the skin-to-skin contact [47]. Reflexologists also believe that the application of deep pressure on certain reflex points of the sole and palm may break any calcium crystals and uric acid accumulated in nerve endings may cause blockages and induces pain [48]. Furthermore, reflexology also results in body relaxation and stimulation of any blocked nerve endings. These may propel any sluggish glands or organs to regain their normal functioning [49]. There is still ambiguity regarding the theories and mechanism of action of foot reflexology for labour pain, as compared to that for general pain. Nonetheless, it is plausible to believe that reflexology techniques would have similar physiological effects for labour pain that bring about a sense of wellbeing, analgesia and subsequently the perception of pain relief through control gate [38].

Massage therapy is another type of the commonly used Complementary and Alternative Methods (CAM) for the promotion of health and wellbeing [36]. Massage produces a short-lived analgesic effect by activating the 'pain gate' mechanism [50]. Massage works as a potent mechanical stimulus and it is a particularly effective trigger for the pain gate process. A longer-lasting pain control appears to be mediated mainly by the descending pain suppression mechanism by activation of descending efferent pathways [51]. The inhibition of pain-transmission neurons is a combination of the physiological and neurological mechanisms and it is commonly activated by noxious stimulation [52]. Figure 1 summarized the possible mechanisms of massage [53].

The three aforementioned therapies (i.e. BRM) for labour pain management have been shown to influence the secretion of certain stress hormones such as the cortisol, adrenocorticotropic hormone (ACTH), and oxytocin [40,54–56]. endorphins [57]. [56–60]. Endogenous oxytocin is a key component in the molecular pathways that buffer reaction to stress and decreases sensitivity to pain and inflammation[61] and Cortisol is an important hormone released during stressful conditions [40].

Significance of this clinical trial

Many studies have reported that not all pharmacologic and non-pharmacologic methods on their own would be able to eliminate labour pain satisfactorily. Despite the intervention, some mothers still endure some pain, anxiety, prolonged labour and suffer from negative maternal and perinatal consequences [5,15,16]. From the perspective of complementary management, BRM are the techniques with the highest potential in managing pain and anxiety for primigravidae. Other systematic reviews have also concluded that CAM

interventions to manage pain and anxiety during labour were often poorly executed and present with biases, thus resulting in low quality of evidence [62–65] with no strongly supported evidence [66,67].

Therefore, there is a need for a rigorous and robust trial to examine the effect of the combined intervention of BRM on labour pain, anxiety, labour duration, satisfaction, stress hormones, and neonatal outcome among the primigravidae using multiple relevant outcome measures.

METHODS AND DESIGN

This study aims to investigate the combined effect of breathing, reflexology and back massage on labor pain, duration of labor, anxiety, maternal satisfaction, stress hormones, and new-born outcome among primigravidae in Saudi Arabia. The specific objectives are 1) to compare the effect of the combined breathing exercise, foot reflexology, and back massage (intervention) on labor pain intensity, anxiety level, duration of labor, maternal satisfaction, stress hormones, and neonatal outcome compared to the standard midwifery care (control), 2) to identify the predictors of pain, anxiety, duration of labor, the satisfaction of mother, and neonatal outcome from the baseline sociodemographic and obstetric characteristics.

Study Design

The study design will be a single-blinded parallel randomised controlled trial (RCT), in which the participants are randomly assigned to receive either the BRM intervention or control care.

Study Setting

This study will be conducted in the Makkah Maternity and Children Hospital, a governmental maternity hospital in Makkah, Saudi Arabia which provides only maternal and child health services. The hospital is a tertiary-level referral hospital with special services for paediatrics, gynaecology, and obstetrics services [68]. In Saudi Arabia, almost all tertiary hospitals, including our study site, offer systemic pharmacologic agents, either intravenous or intramuscular analgesics to manage pain during labour [69] however, non-invasive and non-pharmacological methods of pain relief during labour are not common practices [69]. To our best knowledge, the combined effect of BRM on primigravidae has not been investigated at any Saudi Arabia hospital prior to this trial.

Participants

The study participants will include primigravidae, age 20- 35 years old, at 37 to 41 weeks of gestation, and in the first stage of labor. The inclusion criteria include singleton pregnancy, cephalic presentation, and regular contraction. In labor, the participants must achieve six centimeters of cervical dilatation, with a minimum of 3 contractions with at least moderate intensity every 10 minutes, in which the duration of the contraction must be between 30-60 seconds.

The exclusion criteria are diagnosed with underlying chronic diseases such as cardiovascular diseases, kidney disease, diabetes, asthma, mental health disorders, epilepsy, or seizure. Those with pregnancy-related diseases such as gestational diabetes, preeclampsia, cephalo-pelvic disproportion, polyhydramnios or oligohydramnios, and

deep venous thrombosis will be excluded. Pregnancy with complications such as placenta praevia, antepartum hemorrhage, fetal distress or put on analgesics other than intramuscular Pethidine (IMP) will not be enrolled in the trial.

Recruitment

Recruitment will be conducted at the antenatal clinic in the trial site. Only those who plan to deliver in the trial hospital's delivery room will be further briefed and assessed of their eligibility. In this hospital, antenatal mothers are given monthly follow-up appointments until 28 weeks' gestation. The frequency increases to 2-weekly until 32 weeks' gestation, before patients are seen weekly until delivery. For this study, we will approach primigravidae between 26 to 34 weeks of gestation in equal numbers based on the gestational weeks. In this way, the numbers of expected deliveries will be spread out in the subsequent 2-3 months.

At the antenatal clinic, the principal investigator will provide general health education about pain management during labor. The participant information sheet of this RCT will be provided for the eligible patients. If they are interested to participate, they will sign a written consent form and they will be identified through a unique stamp on their antenatal cards. When the consented participants arrive in the labour room for delivery, they will be re-evaluated for the eligibility.

Randomisation

Since IMP is a commonly prescribed analgesic in labour and it may have substantial effects on the primigravidae and neonates, randomisation will be stratified according to the

administrative status of IMP. This will ensure the same numbers of primigravidae with and without IMP in the intervention and control groups. To achieve this, we use a block of size 4 with a 1:1 allocation ratio, leading to a possibility of 6 permutations. All possible block sequences will be randomly generated with the help of free software from the internet https://www.sealedenvelope.com/simple-randomiser/v1/. A random list will be created after the sample size number, treatment groups, block sizes, list length, and stratification factors are entered into the software. The order of the subjects will be used by the research coordinator who is stationed in the delivery room to conduct the random group allocation for primigravidae in labour who have achieved a cervical dilation of 6 cm. The principal investigator, outcome assessors, and masseuses in this trial are not involved in the allocation of interventional groups. Figure 2 outlines the CONSORT flow diagram.

Data Collection

Every questionnaire will be coded with a unique number. Data collection in the delivery room will be facilitated by the trained research coordinator and two outcome assessors. The outcome assessors will be assigned to the same control or the intervention group on the same day. Once the form is completed by the outcome assessors, it will be kept by the research coordinator in a safe location in the delivery room.

Throughout all the outcome assessment time points, a masseuse will be present in the delivery room of both the intervention and control groups. For the intervention group, the primigravidae in labour will receive the BRM intervention by the masseuse. However, for the control group, the practicing midwife will perform the routine labour care in the presence of a masseuse such as touch therapy, ensuring the mother lying on the left side,

and providing encouragement and counselling. The outcome assessor will measure and assess at the same time points in both the intervention and control groups. Both the intervention and the control groups will be equipped with the similar extra equipment. This blinding effort is to further minimize biases during the outcome assessment. However, blinding of the participants will be impossible because the nature of the intervention does not allow to be applied.

Interventions

The BRM intervention consists of 5 minutes of breathing exercise followed by 10 minutes of foot reflexology on each sole and 35 minutes of continuous massage over the lower limbs and back. And the masseuse will allow the primigravidae for moving and changing her position during intervention time and answer any question or inquiry. Table 1 provides a detailed procedure of the BRM intervention. As for the control group, the primigravidae in labour will receive routine practice.

Training for the research team members

A total of 13 research assistants will be recruited and trained for the intervention and data collection from June to December 2019 (Figure 4). They will be given the BRM training for one week by the principal investigator who has completed the professional massage training by a certified training center in Malaysia (Tim Body Care Training Centre 1403695-D).

Study Outcomes and Measures

There are nine outcomes comprising of two primary outcomes and seven secondary outcomes. The two primary outcomes are pain intensity and anxiety level (See Table 2).

In this study, the pain intensity will be measured multiple times during and after contraction (Figure 3a). It will first be measured at baseline before the intervention. During the intervention, the pain intensity will be measured after breathing exercise and foot reflexology therapy (after 25 minutes from the start of the intervention) followed by another assessment halfway through the massage therapy (after 45 minutes) during and after contraction. Upon completion of the intervention, the measurement will be taken immediately followed by twice hourly thereafter during the first stage of labour. The pain will be measured for every participating primigravidae in both intervention and control groups. For the control group, the pain intensity will be measured, first at baseline before the intervention time at 6 cm. During the intervention time, the pain intensity will be measured after 25 minutes from the start of the intervention time, followed by another assessment after 45 minutes, during and after contraction. Upon completion of the intervention time, the measurement will be taken immediately followed by twice hourly thereafter during the first stage of labour (Figure 3b).

The ASPWL will be used to assess anxiety during labour. The anxiety level will be measured at cervical dilatation of 6cm, after the completion of the interventions, and twice every 60 minutes during the first stage of labour. For the control group, the assessment will be performed when the cervix is 6 cm, after one hour (synchronized to the completion of

the intervention in the intervention group), and twice every 60 minutes during the first stage of labour (Figure 3b).

The secondary outcomes measured in the RCT include maternal stress hormones level, maternal VS, duration of labour, maternal satisfaction, FHR, and neonatal Apgar score. (See Table 3).

The stress hormones level will be measured again one and a half hour after the patient has reached 6 cm of cervical dilatation. Blood samples will again be taken by midwives on duty in the delivery room. This occurs after the BRM intervention in the intervention group, and the same will occur at the same timing in the control group. The blood sample will be sent to a laboratory in the hospital immediately by the research coordinator.

The maternal V/S and FHR will be collected twice at 6cm cervical dilatation and immediately post-BRM for intervention group, and the same data will be collected at the timing for the control groups.

The Apgar Scores (taken from the delivery room medical record) and maternal satisfaction will be measured only once at the end of the childbirth before the transfer of the mother from the delivery room to postnatal wards.

Sample size

The sample size estimation was based on a review of similar literature on pain and anxiety as outcomes [70] and calculated using G*power free software [70]. We estimated the effect size

of 0.6 on anxiety mean score reduction in the intervention group compared to the control [70] as this gives a larger required sample size compared to that based on the primary outcome of pain. Thus, with the power of 95% at α error 0.05, the required sample size is 128 for the two groups. It is further inflated to 154 with a 20% attrition rate. Therefore, a minimum number of 77 primigravidae will be recruited for each group.

Statistical analysis

Data will be entered by a blinded enumerator. The database will be checked for accuracy before analysis. The principal investigator has the overall responsibility for compilation, maintenance, and management of the study database. The analysis will be performed using IBM Statistical Package for Social Science (SPSS) version 25.

Descriptive statistical analysis will be performed according to the distribution of the data, using means and standard deviations for data with normal distribution, and median and inter-quartile ranges for data that are not normally distributed. Normality testing will be conducted for all continuous variables using different methods such as Histogram and p-p plot. Categorical variables will be reported in frequencies and percentages.

The differences between the groups and times level will be analysed using a mixed model or Generalised Linear Mixed Model (GLMM). GLMM is appropriate where repeated measurements are made on the same statistical units. GLMM is also used to accommodate non-normal distribution in outcome data. The variables of time in a categorical form, intervention group, a group*time interaction, and the baseline random part of the model will include a random intercept and an unstructured correlation matrix for the correlation

of measurements within pregnant women. The fixed part of the model will include pain score whereby the difference in pain score at every time point will be tested using a linear contrast. We will take the pain intensity measured with PBI and VAS at one-hour post intervention as the main co-primary outcomes. This is because the effects of the massage and reflexology are still observable and fairly compared to the control group [44,51].

Any significant baseline imbalances will be adjusted for in the analysis. If necessary, multiple imputations will be conducted for the missing data. A calculated 95% confidence interval and two-sided α of 0.05 will be used to test significance. In addition, we will analyze PBI and VAS at same time points and measure the agreement between PBI and VAS by using the Spearman correlation coefficient and interclass correlation. We will analyse other outcomes in the same statistical strategy as mentioned above. Additionally, we will conduct time series analyses to examine the patterns of change in the outcomes between the two groups and after BRM intervention.

Independent effect of socio-demographic and obstetric characteristics on each primary and secondary outcome at one-hour post-intervention will be analysed using the multiple linear regression analyses.

Discussion

There are different types of complementary therapies that have been shown to be beneficial to reduce or alleviate labour pain but the evidence is scarce on the effects of combined therapies [71]. Safe and efficient pain management is important for pregnant women and their families [18]. Therefore, we design this trial to study the effects of BRM on labour pain and

other psychological and physiological impacts among the primigravidae. The study protocol for an RCT is to determine the combined effect of BRM on the intensity of pain and level of anxiety in primigravidae during the first stage of labour. Additional outcomes that will be assessed include the maternal satisfaction, stress hormones, maternal VS, FHR, and neonatal Apgar score.

In this study, we will assess the outcomes using a mixture of subjective and objective tools. For example, pain intensity and anxiety levels are subjective measurements, they are subjective due to the personal feelings and judgment of the respondents. Duration of labour, neonatal Apgar score, and maternal stress hormones level of ACTH, cortisol, and oxytocin will be the objective measurements. This is one of the strengths of our study. These stress hormones are the objective outcomes that will indicate the stress response to the BRM intervention conducted on the primigravidae.

Some of the tools used in this study such as VAS might not be the gold or referent standard to measure labour pain outcome but this is one of the multiple outcomes and alternative ways of measuring the effectiveness of BRM. VAS is a commonly used graphic rating method [72]. However, VAS has its inconsistency of results and has ceiling effect [73,74]. Recognizing this inadequacy, we will ensure the participants understand the VAS scoring at admission to the delivery room before they are asked to indicate their pain level later, and the labour pain outcome will be measured by two different methods and multiple measurements will be taken during and after contraction, before and after the intervention.

As alluded to, we will complement VAS with pain intensity assessment using the PBI [70] to be rated by outcome assessors. There will also be other outcomes that are related to the maternal response to pain, which are the anxiety level and maternal stress hormones [75].

There are several other limitations in this study. Firstly, the intervention will be performed for one hour during which it may be interrupted by routine medical care such as regular vaginal examinations, VS measurements, and fetal heart monitoring. However, we believe that this will not reduce the effect of BRM intervention, because we can start the BRM before or after labour care routine. Secondly, the process of labour and birthing is unpredictable even if the participants are low-risk pregnant women. In certain instances, the process of the intervention might not go well as planned and this may reduce the sample size. Some patients may end up needing a caesarean section due to various reasons and some may suffer from other obstetric complications during delivery. As a result, we have inflated the sample size accordingly. Apart from that, results from this study will not be generalisable to multigravidae as we include only primigravidae. Nevertheless, we believe primigravidae will benefit the most from the intervention as they are likely to experience a higher level of labour pain and a longer duration of the labour compared to multigravidae.

Also, the intervention will be applied only once and only during the first stage of labour even though the first stage of labour among primigravidae take approximately 8-12 hours. By timing the intervention after cervical dilation of 6 cm and above, the effect of the combined BRM could exert its most influences if there is any on the labour experience of the primigravidae and neonatal outcome because this period is believed to be with the highest levels of labour pain.

This study will assess the anxiety level of pregnant mothers. Unlike the labour pain, the level of anxiety can be affected by the individual characteristics, previous life experience, and other environmental causes [76]. However, we believe that these factors may not play a significant role after effective randomisation.

Apart from the actual labour experience, there are a few other external factors that may affect the maternal satisfaction, such as the delivery room services, the health of the baby, the gender of the child, family support, and other psychosocial factors. As satisfaction is a multi-dimensional and complex feeling, it is difficult to measure with a single tool and to narrow it down to only the first stage of labour.

It is understood that a birthing process is a natural event, especially for low-risk women. Thus, the management of labour should be in a supportive manner with minimal or no interferences. This study will provide good-quality evidence on the effects of the combined BRM for labor pain management. These findings will be important for primigravidae and their family members during the decision making about labour pain management.

Acknowledgements

The authors would like to acknowledge the assistance provided by Um-Al-Qura University, the Research Department in the Directorate of Health Affairs, Makkah Region, and Saudi Arabia Culture Mission in Saudi Arabia.

Author Contributions

KB drafted, formulated, and submitted the manuscript. All authors MHR, AHI, LK & BHC contributed to the study designs, read, revised, and approved the research protocol critically for important intellectual content and helped to draft the final manuscript. All authors

approved the final manuscript for submission. Authorship eligibility is in accordance with the International Committee of Medical Journal Editors (ICMJE) guidelines.

Funding

This work was supported by the Umm Al-Qura University and Saudi Arabia Culture Mission (SACM). The author (KB) is a student who owns a Financial Guarantee, which covers the study and research process. The Financial Guarantee will cover all the research's payments. The funders will not be involved in the study design, data collection, analysis and interpretation of the data and writing of the manuscript.

Competing Interest

The authors declare that they have no competing interests.

Patient Consent for Publication

Not applicable since this is a study protocol.

Availability of Data and Materials

The datasets will be available from the corresponding author for reasonable purposes by healthcare professionals, clinicians or scientists in the related fields. Deidentified and anonymised participant data for all the outcomes will be shared once the results have been published and will be made available for as long as possible. Data use will be advised to refer to the published study protocol and trial register.

Ethics Approval and Consent to Participate

Ethics approval has been obtained from the Ethical Committee for Research Involving Human Subjects of the Ministry of Health in the Saudi Arabia (H-02-K-076-0319-109) on 14/April/2019. Additional administrative approvals will be requested from the medical director of Makkah Maternity and Children Hospital.

Reference

1. Gibson E. Women's expectations and experiences with labour pain in medical and midwifery models of birth in the United States. *Women and Birth*. 2014;27:185–9. https://doi.org/10.1016/j.wombi.2014.05.002.
2. Beigi NMA, Broumandfar K, Bahadoran P, et al. Women's experience of pain during childbirth. *Iran J Nurs Midwifery Res* 2010;15:77–82.
3. Devilata T, Swarna S. Effectiveness of pre delivery preparation on anxiety among Primigravida mothers at maternal child health centre Tirupati, AP, India. *IOSR J Nurs Heal Sci* 2015;4:19-24. https://doi.10.9790/1959-04651924.
4. Aksoy M, Aksoy AN, Dostbil A, et al. The Relationship between Fear of Childbirth and Women ' s Knowledge about Painless Childbirth. *Obstet Gynecol Int* 2014;2014:7. http://dx.doi.org/10.1155/2014/274303
5. Nystedt A, Hildingsson I. Diverse definitions of prolonged labour and its consequences with sometimes subsequent inappropriate treatment. *BMC Pregnancy Childbirth* 2014;14:233. https://doi.org/10.1186/1471-2393-14-233
6. Hanjani SM, Tourzani ZM, Shoghi M. The Effect of Foot Reflexology on Anxiety , Pain , and Outcomes of the Labor in Primigravida Women. Acta Med Iran. 2014;53:507–511.
7. Li W, Zhang H, Ling Y, et al. Effect of prolonged second stage of labor on maternal and neonatal outcomes. *Asian Pac J Trop Med* 2011;4:409–411. https://doi.org/10.1016/S1995-7645(11)60114-4
8. Neal JL, Lamp JM, Buck JS, et al. Outcomes of Nulliparous Women with Spontaneous Labor Onset Admitted to Hospitals in Pre-active versus Active Labor. *J Midwifery*

Womens Heal 2014;59:28–34. doi:10.1111/jmwh.12160.Outcomes

9. Kjærgaard H, Olsen JØRN, Ottesen B, et al. Incidence and outcomes of dystocia in the active phase of labor in term nulliparous women with spontaneous labor onset. *Acta Obstet Gynecol* 2009;88:402-407. doi:10.1080/00016340902811001
10. Lowe NK. A Review of Factors Associated With Dystocia and Cesarean Section in Nulliparous Women. *J Midwifery Women's Heal* 2007;52:216–228. doi:10.1016/j.jmwh.2007.03.003
11. Shields SG, Ratcliffe SD, Fontaine P, et al. Dystocia in nulliparous women. *Am Fam Physician* 2007;75:1671-1678.
12. Garthus-Niegel S, Knoph C, von Soest T, et al. The Role of Labor Pain and Overall Birth Experience in the Development of Posttraumatic Stress Symptoms: A Longitudinal Cohort Study. *Birth* 2014;41:108–115. https://doi.org/10.1111/birt.12093
13. Peeler S, Stedmon J, Chung MC, et al. Women's experiences of living with postnatal PTSD. *Midwifery* 2018;56:70–78. https://doi.org/10.1016/j.midw.2017.09.019
14. Boryri T, Noori NM, Teimouri A, et al. The perception of primiparous mothers of comfortable resources in labor pain (a qualitative study). *Iran J Nurs Midwifery Res* 2016;21:239–246. https:// doi.org/10.4103/1735-9066.180386
15. Størksen HT, Garthus-niegel S, Adams SS, et al. Fear of childbirth and elective caesarean section : a population-based study. *BMC Pregnancy Childbirth* 2015;15:221. https://doi.org/10.1186/s12884-015-0655-4
16. Stoll KH, Hauck YL, Downe S, et al. Preference for cesarean section in young nulligravid women in eight OECD countries and implications for reproductive health education. *Reprod Health* 2017;14:116. https://doi.org/10.1186/s12978-017-0354-x

17. El-Aziz SNA, Mansour SE, Hassan NF. Factors associated with fear of childbirth: It's effect on women's preference for elective cesarean section. *J Nurs Educ Pract* 2017;7:133–45. https://doi.org/10.5430/jnep.v7n1p133.

18. Lowe NK. The Pain and Discomfort of Labor and Birth. *J Obstet Gynecol Neonatal Nurs* 1996;25:82–92. https://doi.org/10.1111/j.1552-6909.1996.tb02517.x

19. Rayburn WF, Zuspan FP. Drug therapy in obstetrics and gynecology. 3rd ed. St. Louis:Mosby; 1992.

20. Ullman R, Smith LA, Burns E, et al. Parenteral opioids for maternal pain management in labour. Cochrane Database *Syst Rev* 2010;9. https://doi.org/10.1002/14651858.CD007396.pub2

21. Pereira RR, Kanhai H, Rosendaal F, et al. Parenteral Pethidine for labour pain relief and substance use disorder : 20-year follow-up cohort study in offspring. *BMJ Open* 2012;2:e000719. http://dx.doi.org/10.1136/bmjopen-2011-000719

22. Smith LA, Burns E, Cuthbert A. Parenteral opioids for maternal pain management in labour. Cochrane Database *Syst Rev* 2018;6. https://doi.org/10.1002/14651858.CD007396.pub3

23. Simkin P. Reducing Pain and Enhancing Progress in labor : A Guide to Nonpharmacologic Methods for Maternity Caregivers. *Birth* 1995;22:161–71. https://doi.org/10.1111/j.1523-536X.1995.tb00693.x

24. Cook A, Wilcox G. Pressuring Pain: Alternative Therap for Labor Pain Management. AWHONN *Lifelines* 1997;1:36–41. https://doi.org/10.1111/j.1552-6356.1997.tb00929.x

25. Jones LV. Non-pharmacological approaches for pain relief during labour can improve

maternal satisfaction with childbirth and reduce obstetric interventions. *Evid Based Nurs* 2015;18:70. http://dx.doi.org/10.1136/eb-2014-101938

26. Busch V, Magerl W, Kern U, et al. The Effect of Deep and Slow Breathing on Pain Perception , Autonomic Activity , and Mood Processing -An Experimental Study. *Pain Med* 2012;13:215–28. https://doi.org/10.1111/j.1526-4637.2011.01243.x
27. Thomas ME, Dhiwar MS. Effectiveness of Patterned Breathing Technique in Reduction of Pain During First Stage of Labour Among Primigravidas. Sinhgad E-*Journal Nurs* 2011;1:6–8.
28. Kaur K, Rana AK, Gainder S. Effect of video on ' Breathing Exercises during labour ' on Pain Perception and Duration of Labour Among Primigravida Mothers. *Nurs Midwifery Res Journa* 2013;9:1–9.
29. El-refaye GE, El Nahas EM, Ghareeb HO. Effect of kinesio taping therapy combined with breathing exercises on childbirth duration and labor pain : a randomized controlled trial. *Bull Fac Phys Ther* 2016;21:23–31. https:// doi.10.4103/1110-6611.188026
30. Chuang LL, Lin LC, Cheng P, et al. Effects of a relaxation training programme on immediate and prolonged stress responses in women with preterm labour. *J Adv Nurs* 2011;68:170–80. https://doi.org/10.1111/j.1365-2648.2011.05765.x
31. Akbarzadeh M, Sharif F, Zare N. The Reduction of Anxiety and Improved Maternal Attachment to Fetuses and Neonates by Relaxation Training in Primigravida Women. *Women's Heal Bull* 2014;1:e18968. https://doi.org/10.17795/whb-18968.
32. Nattah FM, Abbas WAK. Assessment of Level of Pain and its Relation with Breathing Exercise in the First Stage of Labour among Primi Mothers at Hilla Teaching Hospital. *Eur J Sci Res* 2016;135:121–8.

33. Yuksel H, Cayir Y, Kosan Z, et al. Effectiveness of breathing exercises during the second stage of labor on labor pain and duration : a randomized controlled trial. *J Integr Med* 2017;15:456–61. https://doi.org/10.1016/S2095-4964(17)60368-6

34. Mathew AM, Francis F. Effectiveness of Foot Refl exology in Reduction of Labour Pain among Mothers in Labour Admitted at PSG Hospital, Coimbatore. *Int J Nurs Educ* 2016;8:11–5. https://doi.org/10.5958/0974-9357.2016.00081.7

35. Moghimi-Hanjani S, Mehdizadeh-Tourzani Z, Shoghi, M. The effect of foot reflexology on anxiety, pain, and outcomes of the labor in primigravida women. *Acta Med Iran* 2015;*53*:507-511.

36. Cohen M. The Effectiveness of Massage Therapy A Summary of Evidence-Based Research. Melbourne:Australian Associaiton of Massage Therapy;2011.

37. Dolatian M, Hasanpour A, Montazeri S, et al. The effect of reflexology on pain intensity and duration of labor on primiparas. *Iran Red Crescent Med J* 2011;13:475–479.

38. Valiani M, Shiran E, Kianpour M, et al. Reviewing the effect of reflexology on the pain and certain features and outcomes of the labor on the primiparous women. *Iran J Nurs Midwifery Res* 2010;15:302–310.

39. Baljon K, Romli MH, Ismail AH, et al. The Effectiveness Of Complementary And Alternative Medicine Of Massage And Reflexology In Managing Pain And Anxiety Among Primigravidas In Labor: A Systematic Review.[in preparation for submission to a journal]

40. Field T, Hernandez-Rief M, Diego M, et al. Cortisol decreases and serotonin increases following massage therapy. *J Neurosci* 2005;115:1397–413.

https://doi.org/10.1080/00207450590956459

41. Crowe K, von Baeyer C. Predictors of a Positive Childbirth Experience. *Birth Iss Perinat C* 1989;16:59–63. https://doi.org/10.1111/j.1523-536X.1989.tb00862.x
42. Ma X, Yue ZQ, Gong ZQ, et al. The effect of diaphragmatic breathing on attention, negative affect and stress in healthy adults. *Front Psychol* 2017;8:1–12. https://doi.org/10.3389/fpsyg.2017.00874
43. Bordoni B, Purgol S, Bizzarri A, et al. The Influence of Breathing on the Central Nervous System. *Cureus* 2018;10:1–8. https://doi.org/10.7759/cureus.2724
44. Tiran D, Chummun H. The physiological basis of reflexology and its use as a potential diagnostic tool. *Complement Ther Clin Pract* 2005;11:58–64. https://doi.org/10.1016/j.ctnm.2004.07.007
45. Tappan FM, Benjamin PJ. Tappan's handbook for healing massage techniques. Classic, Holistic, and Emerging Methods. 3rd Ed. Stamford, Conn.: Appleton & Lange.; 1998.
46. Tiran D, Evans M. Theoretical background to structural reflex zone therapy. Pract. Manag. Pain; 2010.
47. Embong NH, Soh YC, Ming LC, et al. Revisiting reflexology: Concept, evidence, current practice, and practitioner training. *J Tradit Complement Med* 2015;5:197–206. https://doi.org/10.1016/j.jtcme.2015.08.008
48. Poole H, Glenn S, Murphy P. A randomised controlled study of reflexology for the management of chronic low back pain. *Eur J Pain* 2007;11:878–87. https://doi.org/10.1016/j.ejpain.2007.01.006
49. Keet L. Reflexology Bible: The Definitive Guide to Reflexology (Godsfield Bible Series). First Edit. London,Great Britain: Octopus publishing group; 2008.

50. Roudaut Y, Lonigro A, Coste B, et al. Touch sense: functional organization and molecular determinants of mechanosensitive receptors. *Channels* 2012;6:234–45. https://doi.org/10.4161/chan.22213

51. Goats GC. Massage--the scientific basis of an ancient art: Part 2. Physiological and therapeutic effects. *Br J Sports Med* 1994;28:153–6. http://dx.doi.org/10.1136/bjsm.28.3.153

52. Basbaum AI, Fields HL. Endogenous pain control mechanisms: Review and hypothesis. *Ann Neurol* 1978;4:451–62. http://dx.doi.org/10.1002/ana.410040511

53. Weerapong P, Hume PA, Kolt GS. The mechanisms of massage and effects on performance, muscle recovery and injury prevention. *Sport Med* 2005;35:235–56. http://dx.doi.org/10.2165/00007256-200535030-00004

54. Vakilian K, Keramat A. The Effect of the Breathing Technique With and Without Aromatherapy on the Length of the Active Phase and Second Stage of Labor. *Nurs Midwifery Stud* 2013;2. http://dx.doi.org/10.5812/nms.9886

55. Yılar Erkek Z, Aktas S. The Effect of Foot Reflexology on the Anxiety Levels of Women in Labor. *J Altern Complement Med* 2018;24:352–60. https://doi.org/10.1089/acm.2017.0263

56. Morhenn V, Beavin LE, Zak PJ. Massage Increases Oxytocin and Reduces Adrenocorticotropin Hormone in Humans. *Altern Ther* 2012;18:11–8.

57. Diego MA, Field T. Moderate Pressure Massage Elicits a Parasympathetic Nervous System Response. *Int J Neurosci* 2009;119:630–8. http://dx.doi.org/10.1080/00207450802329605

58. McCullough JE, Liddle SD, Sinclair M, et al. The Physiological and Biochemical

Outcomes Associated with a Reflexology Treatment : A Systematic Review. Evidence-Based Complementary *Altern Med* 2014;2014. http://dx.doi.org/10.1155/2014/502123

59. Mccullough JEM, Liddle SD, Close C, et al. Reflexology: a randomised controlled trial investigating the effects on beta-endorphin, cortisol and pregnancy related stress. *Complement Ther Clin Pract* 2018; 31:76–84.
60. Li Q, Becker B, Wernicke J, et al. Foot massage evokes oxytocin release and activation of orbitofrontal cortex and superior temporal sulcus. *Psychoneuroendocrinology* 2018;101:193–203. http://dx.doi.org/10.1016/j.psyneuen.2018.11.016
61. Bell AF, Erickson EN, Carter CS. Beyond Labor: The Role of Natural and Synthetic Oxytocin in The Transition To Motherhood. *J Midwifery Womens Hea*l 2015;59:35–42. http://dx.doi.org/10.1111/jmwh.12101
62. Hu J, Brettle A, Jiang Z, et al. A systematic review and meta-analysis of the effect of massage therapy in pain relief during labor. *J Nurs* 2017;6:1–14. http://dx.doi.org/10.18686/jn.v6i4.130
63. Huntley AL, Coon JT, Ernst E. Complementary and alternative medicine for labor pain : A systematic review. *Am J Obstet Gynecol* 2004;191:36–44. http://dx.doi.org 10.1016/j.ajog.2003.12.008
64. Ranjbaran M, Khorsandi M, Matourypour P, et al. Effect of Massage Therapy on Labor Pain Reduction in Primiparous Women A Systematic Review and Meta-analysis of Randomized Controlled Clinical Trials in Iran. *Iran J Nurs Midwifery Res* 2017;22:257–61.
65. Smith CA, Levett KM, Collins CT, et al. Massage , reflexology and other manual methods for pain management in labour (Review). Cochrane Database Rev. 2012.

66. Kirkham M. The Midwife-Mother Relationship. 2nd ed. Hampshire: Red Globe Press; 2000.

67. Levett KM, Smith CA, Bensoussan A, et al. The Complementary Therapies for Labour and Birth Study: Making sense of labour and birth – experiences of women, partners and midwives of a complementary medicine antenatal education course. *Midwifery* 2016;40:124–131. http://dx.doi.org/10.1016/j.midw.2016.06.011

68. Ministry of Health Saudi Arabia. Maternity and Children Hospital Makkah. 2013. http://www.testonserver.com/mch/ (accessed November 27, 2018).

69. Altaweli RF, McCourt C, Baron M. Childbirth care practices in public sector facilities in Jeddah, Saudi Arabia: A descriptive study. *Midwifey* 2014;30:899–909. http://dx.doi.org/10.1016/j.midw.2014.03.006

70. Bonnel AM, Boureau F. Labor Pain Assessment : Validity of a Behavioral Index. Pain. 1985;22(1):81–90. https://doi.org/10.1016/0304-3959(85)90150-2

71. Snyder M, Wieland J. Complementary and alternative therapies : what is their place in the management of chronic pain ? *Nurs Clin North Am* 2003;38:495–508. http://dx.doi.org/10.1016/S0029-6465(02)00098-1

72. Hayes M, Paterson D. Experimental development of the graphic rating method. Psychol Bull. 1921;18:98–9.

73. Whitburn LY, Jones LE, Davey M, et al. The nature of labour pain : An updated review of the literature. *Women and Birth* 2018;32:28-38. http://dx.doi.org/10.1016/j.wombi.2018.03.004

74. Wei CK, Leng CY, Lin SKS. The use of the Visual Analogue Scale for the assessment of labour pain: a systematic review. *JBI Database Syst Rev Implement* 2010;8:972–

1015.

75. Woo AK. Depression and Anxiety in Pain. *Br J Pain* 2010;4:8–12. https://doi.org/10.1177/204946371000400103

76. Brook CA, Schmidt LA. Social anxiety disorder: A review of environmental risk factors. *Neuropsychiatr Dis Treat* 2008;4:123–43.

77. Chang M, Wang S, Chen C. Effects of massage on pain and anxiety during labour : a randomized controlled trial in Taiwan. *J Adv Nurs* 2002;38:68-73.

78. Mårtensson L, Bergh I. Effect of treatment for labor pain : Verbal reports versus visual analogue scale scores - A prospective randomized study. *Int J Nurs Midwifery* 2011;3:43–7.

79. Bahammam MA, Hassan MH. Validity and reliability of an Arabic version of the modified dental anxiety scale in Saudi adults. *Saudi Med J* 2014;35:1384. http://dx.doi.org/10.2466/pr0.1997.80.3.947

80. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: Visual analog scale for pain (vas pain), numeric rating scale for pain (nrs pain), mcgill pain questionnaire (mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap). *Arthritis Care Res* 2011;63:S240-S252. doi:10.1002/acr.20543

81. Jensen MP, Karoly P, Braver S. The Measurement of Clinical Pain Intensity : a Comparison of Six Methods. P*ain Res Manag* 1986;27:117–26. https://doi.org/10.1016/0304-3959(86)90228-9

82. Durat G, Çulhacik GD, Doğu Ö, et al. The development of an anxiety assessment scale

for pregnant women in labor. *Saudi Med J* 2018;39:609–14. http://dx.doi.org/10.15537/smj.2018.6.22266

83. Harvey S, Rach D, Stainton MC, et al. Evaluation of satisfaction with midwifery care. *Midwifery* 2002;18:260–7. http://dx.doi.org/10.1054/midw.2002.0317

Figure Legend

Figure 1 Mechanisms of Massage therapy

Figure 2 The CONSORT flow diagram

Figure 3 (a) shows the timeline of outcomes measurement in the intervention group; (b) shows the timeline of outcomes measurement in the control group

Figure 4 Research personnel training and responsibility matrix

Table Legend

Table 1 Steps of the Intervention

Table 2 Summary of Primary Outcomes and Measurement Tools

Table 3 Summary of Secondary Outcomes and Measurement Tools

Table 1 Steps of the Intervention

Steps	Process
1.	Prepare the equipment.
2.	Explain the procedure to the primigravidae & advise her to lay on the left side with a pillow on the side of the stomach.
	Breathing Exercise Intervention for 5 minutes
3.	Ask the primigravidae to perform deep breathing slowly through the nose for two seconds and then consciously release the air during breathing out for another two seconds during contractions.
4.	Rest for 1-3 seconds then repeat the same technique for a total of 5 minutes.
	Reflexology Intervention Technique for 10 minutes on each foot
5.	Put a towel under the left foot and cover the right leg.
6.	Apply warm oil over the left foot and roll it left to right for 5 times.
7.	Press palms on the Achilles heel and knead the ankle for 5 times.
8.	Knead the thumb pads on the central and bottom parts of the heel for 5 times.
9.	Knead the foot following the *CIUW shape on the lateral and intermediate aspects of the foot followed by **MST shape for 5 times.
10.	Press the wooden stick of the reflexology on the toes, forefoot, mid-foot, and hind-foot for 5 times.
11.	Repeat Steps 6-11 on the right foot for 5 times.
	Lower Limbs Massage for 2 minutes 30 seconds on each leg
12.	Effleurage massage on the flexed leg by using two hands whole lower leg for 3 times.
13.	Half effleurage massage from the heel to the popliteal area for 3 times.
14.	Palm and thumb kneading on the gastrocnemius muscle over the lateral & medial sides, followed by the scooping on the gastrocnemius, each step for 3 times.
15.	Thumb kneading on the hamstring muscle over the medial, intermediate, and lateral sides for 3 times.
16.	Repeat Steps 12-17 on the right leg for 3 times.
	Lower Back Massage for 15 minutes
17.	Effleurage massage from the sacrum to the shoulders and deltoids for 3 times.
18.	Thumb kneading & pressure over the lateral sides of the lumbar area of the spine for 3 times.
19.	Apply fist knuckling motion and thumb kneading on the lower back, side by side, for 3 times.
	Upper Back Massage for 15 minutes
20.	Effleurage massage followed by palm kneading from the lumbar region to trapezius laterally for 3 times.

21.	Thumb kneading over both sides of erector spinae, then draining between the ribs towards the armpit areas for 3 times.
22.	Apply squeeze on the deltoid muscle with draining towards the armpit for 3 times.
23.	Apply finger kneading on trapezius muscle, followed by fist scooping for 3 times.
24.	Finally, press on the neck and shoulder area on both sides for 3 times.

*CIUW-shape: C-shape; I-shape; U-shape, and W-shape, **MST-shape: M-shape, S-shape, and T-shape.

Table 2 Summary of Primary Outcomes and Measurement Tools

Primary Outcomes	measurement tools	Psychometric tests	Method of assessment
Pain	PBI	-100% inter-rater reliability -*r* coefficient was 0.45, 0. 50, and 0.44 between PBI and PPI. [70,77]	-assessor-rated [70] -five-category behavioural observation scale
	VAS	-moderate correlation ($r = 0.54$) with the verbal rating and is considered valuable when mixed with other tools [78,79] - 0.97 intraclass correlation coefficient of 24 hours interval test-retest reliability [80]	- self-reported VAS [72] - contains six different coloured parts anchored by two extremes of 'no pain' and excruciating pain - to mark on the line-map by primigravidae [81].
Anxiety	ASPWL	- > 0.8 concordance test content validity index -Kendall's W between the opinions of the experts (W= 0.090; *P*= 0.080) with Cronbach's alpha level of 0.77 [82]. significantly correlated (*r*= 0.369) Beck Anxiety Scale [82]	-questionnaire consists of nine items [82] - a 5-point scale and the higher the mean score the more anxiety

Table 3 Summary of Secondary Outcomes and Measurement Tools

Secondary outcomes	Measurement tools	Method of assessment
Maternal stress hormones level,	Blood sample for ACTH, cortisol, oxytocin	Blood sample will be drawn from the median cubital vein during the insertion of IV cannula (routine care)
Duration of labour,	Partograph	Partograph at two separate time intervals, a sum of labour duration from 3 to 6 cm of cervical dilatation and from 6 cm to delivery of the placenta
Maternal satisfaction,	SSQ [83]	Self-reported 7-point scale (1-7) from "strongly disagree to "strongly agree" with higher scores signifying the higher level of satisfaction
Maternal VS	Thermometer Sphygmomanometer	Recorded on the vital sign monitoring chart and cardiotocograph (CTG)
FHR		Recorded on the vital sign monitoring chart and cardiotocograph (CTG)
Neonatal Apgar score	Apgar score table	Taken from the delivery room medical record

Figure Legend

Figure 1 Mechanisms of Massage therapy

Figure 2 The CONSORT flow diagram

Figure 3 (a) shows the timeline of outcomes measurement in the intervention group; (b) shows the timeline of outcomes measurement in the control group

Figure 4 Research personnel training and responsibility matrix

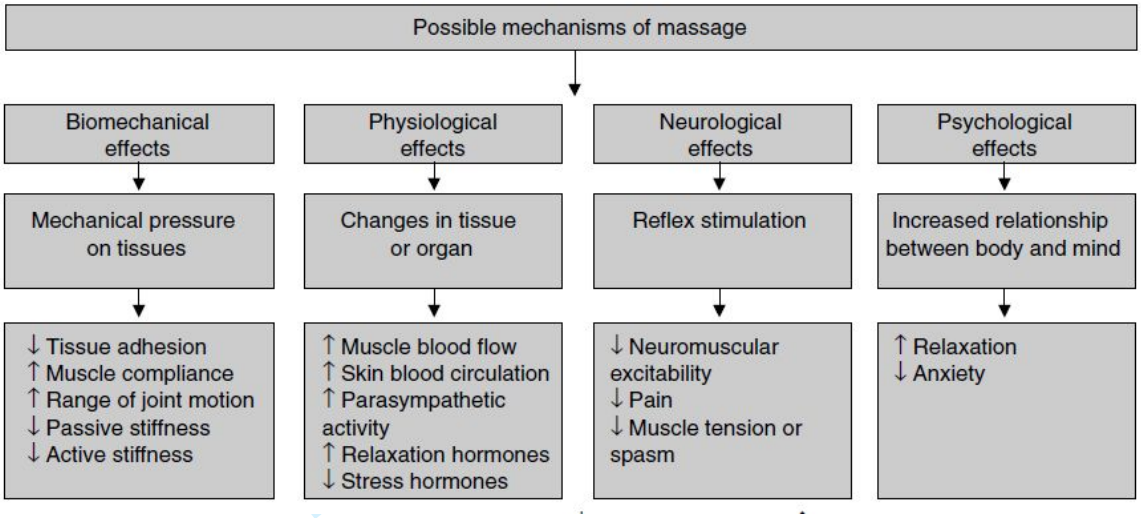
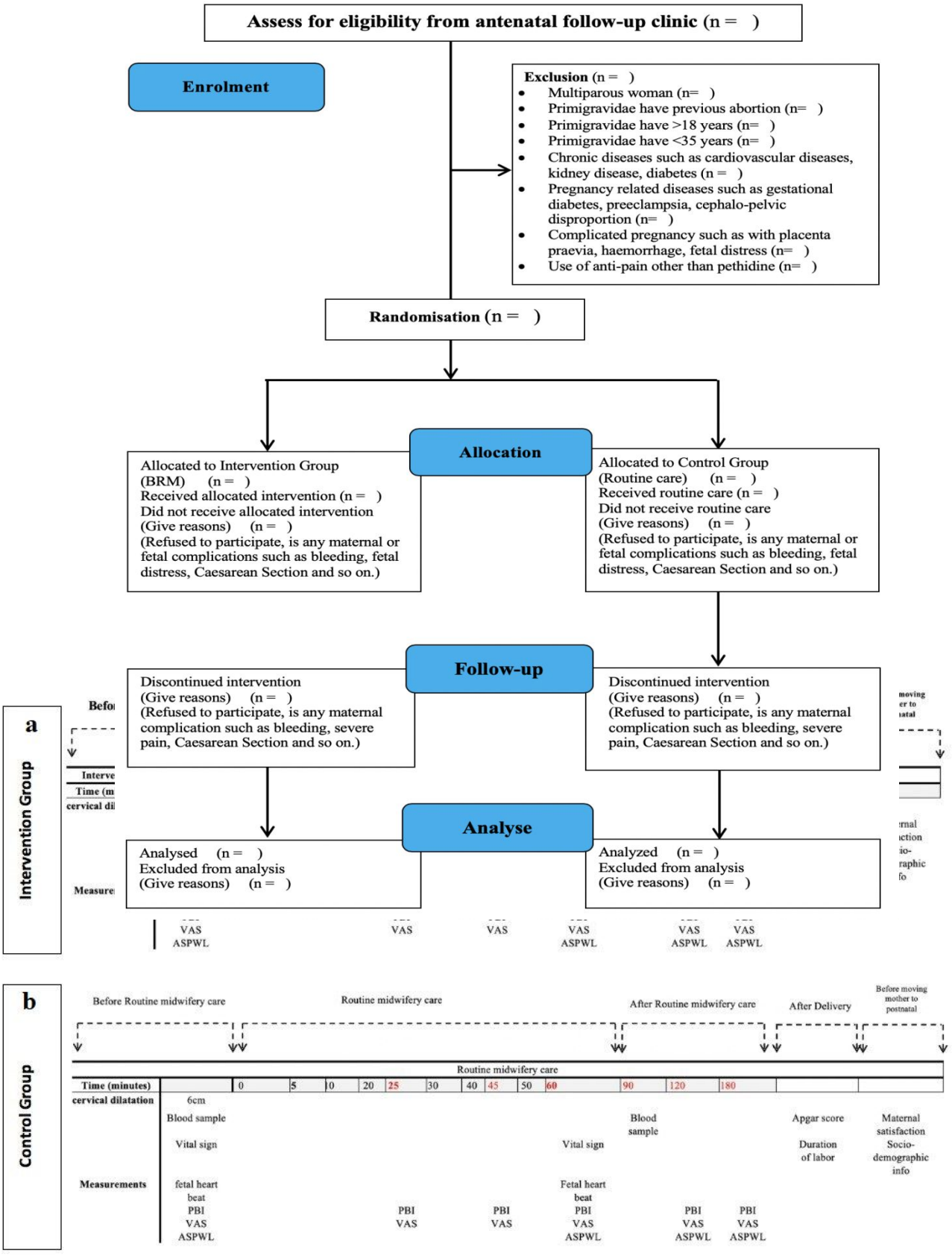


Figure 1 Mechanisms of Massage therapy


Assess for eligibility from antenatal follow-up clinic (n =)
Enrolment
Exclusion (n =)
Multiparous woman (n=)
Primigravidae have previous abortion (n=)
Primigravidae have >18 years (n=)
Primigravidae have <35 years (n=)
Chronic diseases such as cardiovascular diseases, kidney disease, diabetes (n =)
Pregnancy related diseases such as gestational diabetes, preeclampsia, cephalo-pelvic disproportion (n=)
Complicated pregnancy such as with placenta praevia, haemorrhage, fetal distress (n=)
Use of anti-pain other than pethidine (n=)
Randomisation (n =)
Allocation
Allocated to Intervention Group (BRM) (n =)
Received allocated intervention (n =)
Did not receive allocated intervention (Give reasons) (n =)
(Refused to participate, is any maternal or fetal complications such as bleeding, fetal distress, Caesarean Section and so on.)
Allocated to Control Group (Routine care) (n =)
Received routine care (n =)
Did not receive routine care (Give reasons) (n =)
(Refused to participate, is any maternal or fetal complications such as bleeding, fetal distress, Caesarean Section and so on.)
Follow-up
Discontinued intervention (Give reasons) (n =)
(Refused to participate, is any maternal complication such as bleeding, severe pain, Caesarean Section and so on.)
Discontinued intervention (Give reasons) (n =)
(Refused to participate, is any maternal complication such as bleeding, severe pain, Caesarean Section and so on.)
Analyse
Analysed (n =)
Excluded from analysis (Give reasons) (n =)
Analyzed (n =)
Excluded from analysis (Give reasons) (n =)
a
Intervention Group
VAS ASPWL
VAS
VAS
VAS ASPWL
VAS ASPWL
VAS ASPWL
b
Control Group
Before Routine midwifery care
Routine midwifery care
After Routine midwifery care
After Delivery
Before moving mother to postnatal
Routine midwifery care
Time (minutes)
0 5 10 20 25 30 40 45 50 60 90 120 180
cervical dilatation
6cm
Blood sample
Vital sign
Blood sample
Vital sign
Apgar score
Duration of labor
Maternal satisfaction
Socio-demographic info
Measurements
fetal heart beat
PBI
VAS
ASPWL
PBI
VAS
PBI
VAS
Fetal heart beat
PBI
VAS
ASPWL
PBI
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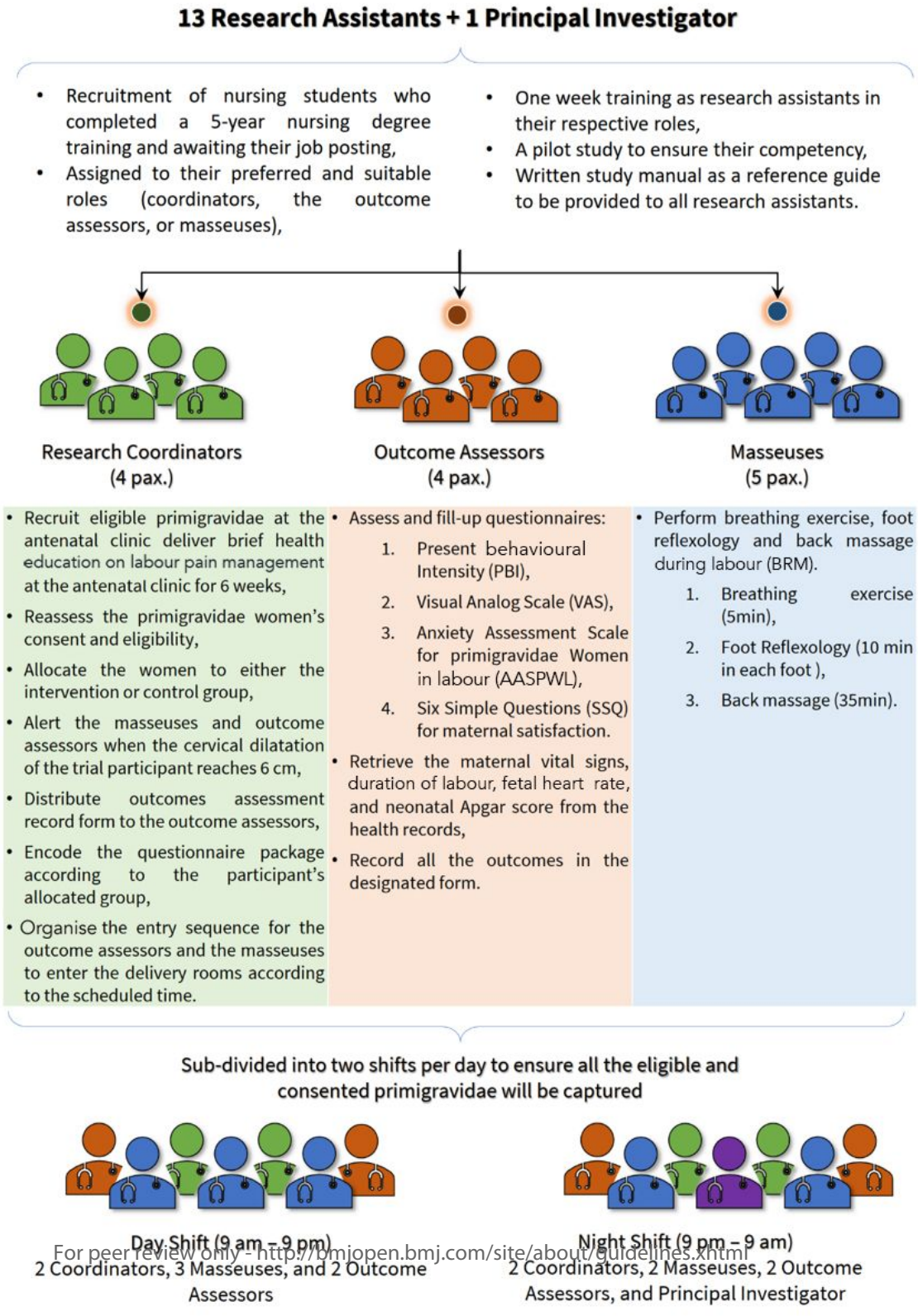
VAS
ASPWL



Figure
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Figure 4 Research personnel training and responsibility matrix

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	4
Protocol version	#3	Date and version identifier	4
Funding	#4	Sources and types of financial, material, and other support	20
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	20
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	1,20
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	20
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team,	N/A

		and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4,5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	5
Objectives	#7	Specific objectives or hypotheses	8
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	9,11
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data	9

		will be collected. Reference to where list of study sites can be obtained	
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9,10
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	12, Table 1
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N/A
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	N/A
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9,10
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical	13,14, table 2, 3

		relevance of chosen efficacy and harm outcomes is strongly recommended	
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 3a, 3b
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	15
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	10,11
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	11

Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	11,12
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Figure 4
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	12,17
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and	12,Figure 4

		validity, if known. Reference to where data collection forms can be found, if not in the protocol	
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	15,16
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	16
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Not mentioned
Methods: Monitoring			

Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	22
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A(no sever adverse effects of BRM recorded)
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	2, 3, 21

Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	2,21
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	3,11
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	3,11
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	20
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	20
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A

Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	2
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	22
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Not mentioned
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	22
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

BMJ Open

Effectiveness of Breathing Exercises, Foot Reflexology and Back Massage (BRM) on Labour Pain, Anxiety, Duration, Satisfaction, Stress Hormones, and New-born Outcomes among Primigravidae during the First Stage of Labour in Saudi Arabia: A Study Protocol for a Randomised Controlled Trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-033844.R1
Article Type:	Protocol
Date Submitted by the Author:	11-Feb-2020
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Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Complementary medicine, Nursing, Emergency medicine, General practice / Family practice, Public health
Keywords:	Breathing exercises, Reflexology, Massage, Primigravidae, Labour pain, Stress hormones

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Effectiveness of Breathing Exercises, Foot Reflexology and Back Massage (BRM) on Labour Pain, Anxiety, Duration, Satisfaction, Stress Hormones and New-born Outcomes among Primigravidae during the First Stage of Labour in Saudi Arabia: A Study Protocol for a Randomised Controlled Trial

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ABSTRACT

Introduction Labour pain is among the severest pains primigravidae may experience during pregnancy. Failure to address labour pain and anxiety may lead to abnormal labour. Despite the many complementary non-pharmacological approaches to coping with labour pain, the quality of evidence is low and best approaches are not established. This study protocol describes a proposed investigation of the effects of a combination of breathing exercises, foot reflexology and back massage (BRM) on the labour experiences of primigravidae.

Methods and analysis This randomised controlled trial will involve an intervention group receiving BRM and standard labour care, and a control group receiving only standard labour care. Primigravidae of 26–34 weeks of gestation without chronic diseases or pregnancy-related complications will be recruited from antenatal clinics. Eligible and consenting patients will be randomly allocated to the intervention or the control group stratified by intramuscular pethidine (IMP) use. The BRM intervention will be delivered by a trained massage therapist. The primary outcomes of labour pain and anxiety will be measured during and after uterine contractions at baseline (cervical dilatation 6 cm) and post-BRM hourly for two hours. The secondary outcomes include maternal stress hormone (adrenocorticotropic hormone, cortisol and oxytocin) levels, maternal vital signs (V/S), foetal heart rate (FHR), labour duration, Apgar scores, and maternal satisfaction. The sample size is estimated based on the between-group difference of 0.6 in anxiety scores, 95% power and 5% α error, which yields a required sample size of 154 (77 in each group) accounting for a 20% attrition rate. The between- and within-group outcome measures will

be examined with mixed-effects regression models, time series analyses and paired t-test or equivalent non-parametric tests, respectively.

Ethics and dissemination Ethical approval was obtained from the Ethical Committee for Research Involving Human Subjects of the Ministry of Health in the Saudi Arabia (H-02-K-076-0319-109) on 14 April 2019, and from the Ethics Committee for Research Involving Human Subjects (JKEUPM) Universiti Putra Malaysia on 23 October 2019, reference number: JKEUPM-2019-169. Written informed consent will be obtained from all participants. Results from this trial will be presented at regional, national and international conferences and published in indexed journals.

Trial registration number and date ISRCTN87414969, registered 3 May 2019

Keywords Breathing exercises, Reflexology, Massage, Primigravidae, Labour pain, Stress hormones.

Article Summary

Strengths and Limitations of the Study

- This single-blind, parallel, randomised controlled trial will explore the combined effects of breathing exercises, foot reflexology and back massage (BRM) on pain and anxiety during labour in healthy primigravidae with a singleton foetus.
- The effects of BRM will also be examined through objective physiological measurement of stress hormone levels and comparison of these levels between groups before and after the intervention.
- The intervention will be applied for one hour and only once during the first stage of labour after cervical dilatation of 6 centimetres.
- Blinding of the primigravidae mothers is not possible, and there may be bias in the self-assessed subjective outcomes such as the Visual Analog Scale.
- The expertise and experience of the nursing graduates who are trained to be the massage therapists is considered an important factor in the quality of treatment provided and this may underestimate the effect of BRM.

Word count 4,907 words

INTRODUCTION

Many primigravidae have reported experiencing various levels of pain during labour and high levels of anxiety about the labour process and its outcomes [1-3]. Anxiety escalating to fear is a common issue related to labour, especially among primigravidae [4, 5]. Other recorded negative perceptions and psychological effects influencing labour experiences include distress and feelings of powerlessness during labour for women and their families [5-7].

When poorly managed, labour pain may lead to severe consequences for women, such as prolonged labour [5, 8], which may increase the risk of foetal distress, head compression, intrauterine foetal death, low Apgar scores and physical injuries to neonates [5, 9]. Prolonged labour results in increased risk of caesarean section, induced labour and assisted delivery using vacuum and forceps [10, 11]. Studies have also reported negative mental impacts on women, sometimes even including postnatal post-traumatic stress disorder [12, 13], and subsequently reduced quality of life [14]. Feelings of anxiety often originate from possible birthing complications about which pregnant women have heard and read [4, 5, 15, 16], and may even result in women refusing normal vaginal delivery and insisting on caesarean sections without medical indications [17]. It is therefore important for healthcare professionals to assist and educate all expectant mothers on labour pain management.

Appropriate labour pain management and interventions are important aspects of obstetric care to ensure optimum outcomes for mothers and babies [18]. Pharmacologic interventions used in the management of labour pain include systemic sedatives, analgesics

and regional anaesthesia [19]. Examples of these analgesics are aerosol and epidural opioids, intramuscular pethidine (IMP) and intravenous sedatives [20, 21]. Some of these are expensive and may be associated with adverse effects on mothers, the labour process and neonates [22]. In contrast, most non-pharmacological methods for labour pain management are simple and non-invasive, and are often cheaper and safer than pharmacological interventions [23-25]. Studies have found that non-pharmacological approaches, particularly breathing exercises, have positive impacts on relief of labour pain [26-28], and anxiety in pregnant mothers [29-31]. This is especially true for Lamaze breathing, deep breathing exercises [26-28, 32, 33], reflexology [34, 35], and massage [36]. Non-pharmacological approaches have been linked to shorter labour duration [37], and improved new-born outcomes [38]. Our systematic review found that massage is beneficial for relieving labour pain [39], and is associated with greater relaxation, higher alertness levels, improved mood and reduced stress hormone (cortisol) levels and anxiety symptoms [40].

Rationale

It is hypothesised that the non-pharmacological approach of labour pain management occurs via the alteration of nociceptive stimuli and modification of the processing of nociceptive input at the central level, resulting in an overall improved sense of comfort and well-being, ultimately leading to stronger coping capabilities by the mothers in labour [41].

The physiological mechanism of breathing is a protective action as it is a fight-or-flight reflex triggered by the central nervous system. Physiologically, deep abdominal breathing stimulates the parasympathetic nervous system. As a result, the blood circulation in

pregnant women will undergo oxygenation, which will trigger the release of endorphins associated with decrease in heart rate and increase in feelings of calmness. At the same time, endorphins can also suppress the sympathetic system, leading to a decrease in the release of stress hormones such as cortisol [42, 43].

As for reflexology, so far there has been no constructive explanation of the underlying mechanism in reducing labour pain [35, 37]. The reflexology therapist will apply pressure many times on specific points of the feet that are energetically connected to certain parts and organs of the body. These include reflex points on the tips of the fingers that reflect the head, brain, and pituitary gland, and are believed to facilitate the secretion of the endogenous endorphins that reduce labour pain, stress, fatigue and anxiety [44, 45]. Pressure on the solar plexus at the border of the upper and middle one-third of the sole is believed to facilitate the functions of the body's nervous system [46]. Pressure on the lower part of the forefoot reflects the heart and lungs. While pressure on the bridge of the foot reflects the liver and kidney and the heel will reflect the lower back, legs, pelvic region uterus, and intestines. The uterine point is believed to be located in the indented region between the inner ankles and the sole [47]. Therefore, it is believed to be helpful during labour. The pressure on toe and heel stimulate the reflex points in the pelvis. The pressure on the middle toe facilitate the cervical dilation and ease uterine contractions [48, 49].

However, there are several postulated theories for its mechanism of action. Firstly, the autonomic-somatic integration theory suggests that the pressure applied to the feet during reflexology compresses the receptors in the cells, thus opening up the ionic channels in the plasma membrane and triggering a local action with the potential to convey messages to

the spinal cord and/or brain [50]. The application of alternating pressure to the feet may also produce predictable reflexive actions within the nervous system and activate the parasympathetic nervous system [51].

Another contemporary method explains that reflexology acts through "sympathetic resonance," in which an energy wave flows between therapist and client, promoting homeostatic balance [52]. This may occur through local enzymatic reactions on receptive fields or through an improved blood supply as a result of local skin temperature changes following the skin-to-skin contact [53]. Reflexologists also believe that the application of deep pressure on certain reflex points of the sole and palm may break any calcium crystals and uric acid accumulated in nerve endings that may cause blockages and induce pain [54].

Reflexology also results in body relaxation and stimulation of any blocked nerve endings, which may propel any sluggish glands or organs to regain their normal functioning [55]. Ambiguity remains regarding the theories and mechanism of action of foot reflexology for labour pain, as compared to that for general pain [35-37]. Nonetheless, it is plausible to believe that reflexology techniques would have similar physiological effects for labour pain that bring about a sense of wellbeing, analgesia and subsequently the perception of pain relief [38]. Figure 1 summarizes the possible mechanisms of Reflexology therapy.

Massage therapy is another type of commonly used Complementary and Alternative Method (CAM) for the promotion of health and wellbeing [36]. Massage is a potent mechanical stimulus that produces a short-lived analgesic effect by activating the 'pain gate' mechanism [56]. Longer-lasting pain control appears to be mediated mainly by the

descending pain suppression mechanism by activation of descending efferent pathways [57]. The inhibition of pain-transmission neurons involves a combination of physiological and neurological mechanisms and it is commonly activated by noxious stimulation [58]. Figure 2 summarizes the possible mechanisms action of massage therapy [59].

The three aforementioned therapies (i.e. BRM) for labour pain management have been shown to influence the secretion of certain stress hormones such as cortisol, adrenocorticotropic hormone (ACTH), and oxytocin (OT) [40, 49, 60, 61], endorphins [61-65]. Endogenous oxytocin is a key component in the molecular pathways that buffer reaction to stress and decrease sensitivity to pain and inflammation [66]; cortisol is an important hormone released during stressful conditions [40].

Significance of this clinical trial

Many studies have reported that not all pharmacologic and non-pharmacologic methods on their own are able to reduce labour pain satisfactorily. Despite the intervention, some mothers still endure some pain, anxiety and prolonged labour, and suffer from negative maternal and perinatal consequences [5, 15, 16]. From the perspective of complementary management, BRM are the techniques with the highest potential for managing pain and anxiety for primigravidae. Systematic reviews have concluded that CAM interventions to manage pain and anxiety during labour have often been biased and/or poorly executed, thus resulting in low quality of evidence [67-70], or no strongly supported evidence [71, 72]. Therefore, there is a need for a rigorous and robust trial to examine the effect of the combined intervention of BRM on labour pain, anxiety, stress hormones, V/S, FHR,

duration of labour, Apgar Scores and maternal satisfaction among the primigravidae using multiple relevant outcome measures.

METHODS AND DESIGN

This study aims to investigate the combined effect of BRM on labour pain, duration of labour, anxiety, maternal satisfaction, stress hormones, and new-born outcome among primigravidae in Saudi Arabia. The specific objectives are 1) to compare the effect of the combined breathing exercise, foot reflexology, and back massage (intervention) on labour pain intensity, anxiety level, duration of labour, maternal satisfaction, stress hormones, and neonatal outcome compared to the standard midwifery care (control); 2) to identify the predictors of pain, anxiety, duration of labour, the satisfaction of mother, and neonatal outcome from the baseline sociodemographic and obstetric characteristics.

Study Design

The study design will be a single-blind parallel randomised controlled trial (RCT), in which participants are randomly assigned to receive either the BRM intervention or control care.

Study Setting

This study will be conducted in the Makkah Maternity and Children Hospital (MCH) in Makkah, Saudi Arabia. The hospital is a tertiary-level, governmental referral hospital with special services for paediatrics, gynaecology, and obstetrics [73]. In Saudi Arabia, almost all tertiary hospitals, including our study site, offer systemic pharmacologic agents, either intravenous or intramuscular analgesics to manage pain during labour [74]; however,

providing non-invasive and non-pharmacological methods of pain relief during labour are not common practices [74]. To our best knowledge, the combined effect of BRM on primigravidae has not been investigated at any Saudi Arabia hospital prior to this trial.

Participants

The study participants will include primigravidae, age 20–35 years old, at 37 to 41 weeks of gestation, and in the first stage of labour. The inclusion criteria include singleton pregnancy, cephalic presentation, and regular contraction. In labour, the participants must achieve six centimetres of cervical dilatation, with a minimum of 3 contractions of at least moderate intensity every 10 minutes, in which the duration of the contraction must be between 30–60 seconds.

The exclusion criteria include diagnosis of underlying chronic diseases such as cardiovascular disease, kidney disease, diabetes, asthma, mental health disorders, epilepsy or seizure; pregnancy-related diseases such as gestational diabetes, preeclampsia, cephalo-pelvic disproportion, polyhydramnios or oligohydramnios or deep venous thrombosis; and pregnancy complications such as placenta praevia, antepartum haemorrhage, fetal distress or being put on analgesics other than IMP.

Patient and Public Involvement

Patients are involved in the questionnaire's face and content validity testing. Based on feedback from the patients in a pilot study, improvement to the questionnaires' approaches and trial processes will be implemented. Patient preferences were not directly obtained

with regard to choosing the BRM intervention; this was based on the principal investigator's practice experience and encounters with pregnant women.

Recruitment

Recruitment will be conducted at the antenatal clinic at the trial site. Only those who plan to deliver in the trial hospital's delivery room will be further briefed and assessed for their eligibility. At this hospital, antenatal mothers are given monthly follow-up appointments until 28 weeks' gestation. The frequency increases to bi-weekly until 32 weeks' gestation; then patients are seen weekly until delivery.

For this study, we will approach primigravidae between 26 to 34 weeks of gestation in equal numbers based on the gestational weeks. This means that about an equal number of primigravidae at week of gestation of 26, 28, 30, 32 and 34 will be recruited in order to spread out the occurrence of labour in the subsequent 2–3 months to increase the feasibility of the BRM intervention. Because participant recruitment and the training of the research team members is estimated to last up to two to three months, women of 34+ weeks gestation cannot be recruited during this period because they will inevitably go into labour before the research preparations are complete.

At the antenatal clinic, the principal investigator will provide general health education about pain management during labour. The participant information sheet of this RCT will be provided for the eligible patients. If they are interested in participating, they will sign a written consent form and will be identified by a unique stamp on their antenatal cards.

When the participants arrive in the labour room for delivery, they will be re-evaluated for the eligibility.

Randomisation

Since IMP is a commonly prescribed analgesic in labour, and may have substantial effects on the primigravidae and neonates, randomisation will be stratified according to the administrative status of IMP. This will ensure the same numbers of primigravidae with and without IMP in the intervention and control groups. To achieve this, we use a block of size 4 with a 1:1 allocation ratio, leading to a possibility of 6 permutations. All possible block sequences will be randomly generated with the help of free software from the internet https://www.sealedenvelope.com/simple-randomiser/v1/. A random list will be created after the sample size number, treatment groups, block sizes, list length, and stratification factors are entered into the software. The order of the subjects will be used by the research coordinator who will be stationed in the delivery room to conduct the random group allocation for primigravidae in labour who have achieved a cervical dilation of 6 cm. The principal investigator, outcome assessors, and massage therapist in this trial will not be involved in the allocation of the interventional groups. Figure 3 outlines the CONSORT flow diagram.

Data Collection

Every questionnaire will be coded with a unique number. Data collection in the delivery room will be facilitated by the trained research coordinator and two outcome assessors. The outcome assessors will be assigned to the control or the intervention group on the same

day. Once the form is completed by the outcome assessors, it will be kept by the research coordinator in a safe location in the delivery room.

Throughout all of the outcome assessment time points, a massage therapist will be present in the delivery room of both the intervention and control groups. For the intervention group, the primigravidae in labour will receive the BRM intervention from the massage therapist. For the control group, the practicing midwife will perform routine labour care such as touch therapy, ensuring that the mother lies on her left side, and providing encouragement and counselling. The outcome assessor will measure and assess both the intervention and control groups at the same time points. Both groups will be equipped with similar extra equipment. This blinding effort is intended to minimize biases during the outcome assessment. However, blinding of the participants will be impossible due to the nature of the intervention.

Interventions

The BRM intervention consists of 5 minutes of breathing exercise followed by 10 minutes of foot reflexology on each sole and 35 minutes of continuous massage over the lower limbs and back. The massage therapist will allow the primigravidae to lie on the left side [75], to move and change her position during the intervention, and answer any question or inquiry. Table 1 provides a detailed explanation of the BRM intervention procedure. As for the control group, the primigravidae in labour will receive routine labour room care.

Training for the research team members

A total of 13 research assistants will be recruited and trained for the intervention and data collection from June to December 2019, (Figure 4). They will be given the BRM training for one week by the principal investigator who has completed the professional massage and reflexology training at a certified training centre in Malaysia (Tim Body Care Training Centre 1403695-D) for six months including training and working.

Study Outcomes and Measures

There are eight outcomes: two primary outcomes and six secondary outcomes. The two primary outcomes are pain intensity and anxiety level (See Table 2). Pain intensity is measured with the Present Behavioural Intensity (PBI) [76,77] and the self-report Visual Analog Scale (VAS) [78-82], while anxiety is measure with Anxiety Assessment Scale for Pregnant Women in Labour (AASPWL) [83].

The outcome assessor will ask the pregnant women to pick a colour on an A-4 sized paper that contains six different coloured parts, from no pain (score 1) to most severe pain (score 6) based on her level of pain [81, 84]. The researcher selected the VAS questionnaire because it is an acceptable tool and relatively easy to administer to women in labour. Pain intensity will be measured at baseline before the intervention, and multiple times during and after contractions (Figure 5a). During the intervention, pain intensity will be measured after the breathing exercise and foot reflexology therapy (after 25 minutes from the start of the intervention), followed by another assessment halfway through the massage therapy (after 45 minutes) during and after contraction. Pain intensity will be measured for every

participating primigravidae in both the intervention and control group. For the control group, pain intensity will be measured first at baseline before the intervention at 6 cm. During the intervention, pain intensity will be measured after 25 minutes from the start of the intervention time, followed by another assessment after 45 minutes, during and after contraction. Upon completion of the intervention, the measurement will be taken immediately, and twice hourly thereafter during the first stage of labour (Figure 5b).

The AASPWL will be used to assess anxiety during labour. The anxiety level will be measured at cervical dilatation of 6cm, after the completion of the interventions, and twice every 60 minutes during the first stage of labour. For the control group, the assessment will be performed when the cervix is at 6 cm, after one hour (synchronized to the completion of the intervention in the intervention group), and twice every 60 minutes during the first stage of labour (Figure 3b).

The secondary outcomes measured in the RCT include maternal stress hormones level, maternal V/S, FHR, duration of labour, neonatal Apgar score, and maternal satisfaction [85] (See Table 3).

The stress hormones level will be measured at baseline, and again one and a half hour after the patient has reached 6 cm of cervical dilatation (Figure 5). Blood samples will again be taken by midwives on duty in the delivery room. This will occur after the BRM intervention in the intervention group (Figure 5a), and at the same time in the control group (Figure 5b). The research assessors will collect an 8 ml blood sample in a plain tube, of which 3 mls is for ACTH, 3 mls for cortisol, and 2 mls for OT hormones; it will be sent immediately to

the MCH laboratory to carefully avoid any haemolysis of the samples. Hormones will be analysed by the sandwich ELISA technique using commercial kits by Cobas e411 Analyzer (HITACHI, USA) for ACTH hormone, and Abbot Architect I200 Analyzer (Abbott, USA) for Cortisol and OT hormones.

Since cortisol levels follow a diurnal variation or circadian rhythm where the hormone levels peak in the morning and fall at night, and vary in accordance with a number of factors including age, time of day, stress level, sample type, laboratory location and the method used for testing [86, 87], we will use a chart from the laboratory to verify the normal cortisol range in the morning, noon, afternoon, evening, or night, and compare these ranges to the blood samples taken to determine whether the blood test results of the participants before and after the intervention are high, normal or low.

ACTH and cortisol levels are interrelated. When the cortisol levels are at their peak, ACTH levels generally fall and vice versa [88]. Hence, it may be understood that ACTH and cortisol have corresponding levels at any given point of time. This provides a relative value for both stress hormones. With regard to OT, the blood sample test for the pregnant woman will be higher if she receives an infusion of OT during intervention [89, 90]. If the events are equal in both groups, we will proceed to the analysis as planned. If the events are many and unequal in both groups, we will either conduct a separate statistical analysis stratified according to the event of OT infusion. If the number of event occurrences is low, we may exclude these participants and analyse the outcome as planned. However, the author will investigate the oxytocin level before and after applying the BRM in addition to childbirth. Oxytocin increases with contraction and hypothetically with and after BRM.

The oxytocin will increase in the second stage, inhibit the Stress hormones, and will increase after apply the BRM.

Maternal V/S and FHR will be collected twice at 6cm cervical dilatation and immediately post-BRM for the intervention group, and the same data will be collected at the same timing for the control groups. The Apgar Scores (taken from the delivery room medical record) and maternal satisfaction will be measured only once at the completion of the childbirth, before the transfer of the mother from the delivery room to the postnatal ward.

Sample size

The sample size estimation was based on a review of similar literature on pain and anxiety as outcomes [76], and calculated using G*power free software [76]. We estimated an effect size of 0.6 on anxiety mean score reduction in the intervention group compared to the control [76], as this gives a larger required sample size compared to that based on the primary outcome of pain. Thus, with the power of 95% at α error 0.05, the required sample size is 128 for the two groups. It is further inflated to 154 to account for a predicted 20% attrition rate. Therefore, a minimum number of 77 primigravidae will be recruited for each group.

Statistical analysis

Data will be entered by a blinded enumerator. The database will be checked for accuracy before analysis. The principal investigator has the overall responsibility for the compilation, maintenance, and management of the study database. The analysis will be performed using IBM Statistical Package for Social Science (SPSS) version 25.

Descriptive statistical analysis will be performed according to the distribution of the data, using means and standard deviations for data with normal distribution, and median and inter-quartile ranges for data that are not normally distributed. Normality testing will be conducted for all continuous variables using different methods such as Histogram and p-p plot. Categorical variables will be reported in frequencies and percentages.

The differences between the groups and times level will be analysed using a Generalised Linear Mixed Model (GLMM). GLMM is appropriate where repeated measurements are made on the same statistical units. GLMM will also be used to accommodate non-normal distribution in outcome data. The variables of time in a categorical form, intervention group, group*time interaction, and the baseline random part of the model will include a random intercept and an unstructured correlation matrix for the correlation of measurements within pregnant women. The fixed part of the model will include pain score, whereby the difference in pain score at every time point will be tested using a linear contrast. We will take the pain intensity measured with PBI and VAS at one-hour post intervention as the main co-primary outcomes. This is because the effects of the massage and reflexology will still be observable, and thus the intervention group can be fairly compared to the control group [50-57].

Any significant baseline imbalances will be adjusted for in the analysis. If necessary, multiple imputations will be conducted for the missing data. A calculated 95% confidence interval and two-sided α of 0.05 will be used to test significance. In addition, we will analyse PBI and VAS at the same time points and measure the agreement between PBI and VAS by using the Spearman correlation coefficient and interclass correlation. We will

analyse other outcomes using the same statistical strategy mentioned above. Additionally, we will conduct time series analyses to examine the patterns of change in the outcomes between the two groups and after BRM intervention.

The independent effect(s) of socio-demographic and obstetric characteristics on each primary and secondary outcome at one-hour post-intervention will be analysed using multiple linear regression analyses.

Discussion

Safe and efficient pain management is important for pregnant women and their families [18], and different types of CAM have been shown to be beneficial to reduce or alleviate labour pain. However, evidence is scarce regarding the effects of combined therapies [91]. Therefore, we designed this trial to study the effects of BRM on labour pain and other psychological and physiological impacts among primigravidae. The study protocol for the RCT is to determine the combined effect of BRM on the intensity of pain and level of anxiety in primigravidae during the first stage of labour. Additional outcomes that will be assessed include stress hormones, maternal VS, FHR, duration labour, neonatal Apgar score, and maternal satisfaction.

In this study, the intervention will be applied only once and only during the first stage of labour even though the first stage of labour among primigravidae takes approximately 8–12 hours. By timing the intervention after cervical dilation of 6 cm, the effect of the combined BRM could exert its greatest influences (if any) on the labour experience of the

primigravidae and neonatal outcome, because this period is believed to accompany the highest levels of labour pain [92, 93].

We will assess the outcomes using a mixture of subjective and objective tools. For example, pain intensity and anxiety levels are subjective measurements, based on the personal feelings and judgments of the respondents. Duration of labour, neonatal Apgar score, and maternal stress hormones level of ACTH, cortisol, and oxytocin are objective measurements that will indicate the stress response to the BRM intervention conducted on the primigravidae. This is one of the strengths of our study.

VAS is one of several ways of measuring the effectiveness of BRM, and is a commonly used graphic rating method [76, 84]. However, VAS might not be the gold standard to measure labour pain, given the inconsistency of its results and its ceiling effect [84, 94]. Recognizing this inadequacy, we will ensure that the participants understand the VAS scoring at admission to the delivery room before they are asked to indicate their pain level later. Labour pain outcome will also be measured via pain intensity assessment using the PBI [76], which will be rated by outcome assessors. Multiple measurements will be taken during and after contraction, and before and after the intervention. There will also be other outcomes, related to maternal response to pain, namely anxiety level and maternal stress hormones [95].

This study has several other limitations. First, the intervention will be performed for one hour, during which it may be interrupted by routine medical care such as regular vaginal examinations, V/S measurements, and FHR monitoring. However, we believe that this will

not reduce the effect of the BRM intervention, because we can start the BRM before or after the labour care routine. Second, the process of labour and birthing is unpredictable even if the participants are low-risk. In certain instances, the process of the intervention might not go well as planned and this may reduce the sample size. Some patients may end up needing a caesarean section, and some may suffer from other obstetric complications during delivery. As a result, we have inflated the sample size accordingly. Third, the results from this study will not be generalisable to multigravidae as we include only primigravidae. Nevertheless, we believe that primigravidae will benefit the most from the intervention as they are likely to experience a higher level of labour pain and a longer duration of labour compared to multigravidae. Fourth, placebo effects can influence patient outcomes after (CAM), resulting in high rates of good outcomes, which may be wrongly attributed to specific treatment effects [96].

We recognise that the expertise and experience level of the reflexologist is an important factor in the quality of treatment provided and this may affect the outcomes of the BRM. The massage therapists and the outcome assessors will be given the appropriate training on the BRM for one week by the principal investigator who attended a professional training and was certified. After the training, they will be tested in a pilot study to ensure their competency in performing the BRM. Additional quality control measures for the outcome assessors are planned, as they will be assigned to the control delivery room or the intervention delivery room on the same day. All of the completed assessment forms will be reviewed and kept by the research coordinator in a safe location in the delivery room.

Any issues on the form such as blank spaces and extreme values will be immediately clarified and resolved.

In addition to labour pain, this study will assess the anxiety level of pregnant mothers. Unlike labour pain, anxiety level can be affected by individual characteristics, previous life experiences, and other environmental causes [97]. However, we believe that these factors will not play a significant role after effective randomisation.

Apart from the actual labour experience, there are a few other external factors that may affect maternal satisfaction, such as the delivery room services, the health of the baby, the gender of the child, family support, and other psychosocial factors. As satisfaction is a multi-dimensional and complex feeling, it is difficult to measure with a single tool and to narrow it down to only the first stage of labour.

It is understood that a birthing process is a natural event, especially for low-risk women. Thus, the management of labour should be conducted in a supportive manner with minimal or no interferences. This study will provide high-quality evidence about the effects of the combined BRM for labour pain management. These findings will be important for hospitals offerings for expectant mothers in providing a rationale for their decisions about which alternative treatments to offer, to primigravidae and their family members during decision making about labour pain management.

Acknowledgements

The authors would like to acknowledge the assistance provided by Um-Al-Qura University, the Research Department in the Directorate of Health Affairs, Makkah Region, and Saudi Arabia Culture Mission in Saudi Arabia.

Author Contributions

KB drafted, formulated, and submitted the manuscript. All authors MHR, AHI, LK & BHC contributed to the study designs, read, revised, and approved the research protocol critically for important intellectual content and helped to draft the final manuscript. All authors approved the final manuscript for submission. Authorship eligibility is in accordance with the International Committee of Medical Journal Editors (ICMJE) guidelines.

Funding

This work was supported by the Umm Al-Qura University and Saudi Arabia Culture Mission (SACM). The author (KB) is a student who owns a Financial Guarantee, which covers the study and research process. The Financial Guarantee will cover all the research's payments. The funders will not be involved in the study design, data collection, analysis and interpretation of the data and writing of the manuscript.

Competing Interest

The authors declare that they have no competing interests.

Patient Consent for Publication

Not applicable since this is a study protocol.

Availability of Data and Materials

The datasets will be available from the corresponding author on reasonable request. The data will be kept for a maximum period of two years from the end of data analysis and will be placed in a sealed envelope that will remain with the primary author. Subsequently, the forms will be destroyed via a shredding machine located at UPM in the presence of my supervisor and some academic staff. The soft copy and record data, as well as the questionnaires and database of hard copy will be deleted, and we will re-setup windows in the computer to destroy the database after a maximum period of two years.

Ethics Approval and Consent to Participate

Ethics approval was obtained from the Ethical Committee for Research Involving Human Subjects of the Ministry of Health in the Saudi Arabia (H-02-K-076-0319-109) on 14 April 2019, and from the Ethics Committee for Research Involving Human Subjects (JKEUPM) Universiti Putra Malaysia on 23 October 2019, reference number (JKEUPM-2019-169). Additional administrative approval will be requested from the medical director of the Makkah Maternity and Children Hospital. The participant information sheet for the pregnant women will be also provided. If they are interested and eligible to participate, pregnant women will sign consent forms. Consent form contains purpose of this study, procedures involved in the research pre and post intervention. They will inform the potential benefits and risk of the intervention research. Participants will be given an affirmation of confidentiality and protection the data collection. The results won't be disseminated to the study participants, except If one of the participants would like to know her results, her mobile number will be taken and a message will be sent.

Patient and Public Involvement

Patients are involved in the questionnaire's face and content validity testing. Based on feedback from the patients in a pilot study, improvement to the questionnaires' approaches and trial processes will be implemented. Patient preferences were not directly obtained with regard to choosing the BRM intervention; this was based on the principal investigator's practice experience and encounters with pregnant women. However, the patients will be involved in the recruitment to and conduct of the study. They will attend antenatal class and agreement by consent to share in this study. Also, they will answer all questionnaires pre and post the intervention. In addition, they will need to agree to BRM as the intervention.

Reference

1. Gibson E. Women's expectations and experiences with labour pain in medical and midwifery models of birth in the United States. *Women and Birth*. 2014;27:185–9. https://doi.org/10.1016/j.wombi.2014.05.002.

2. Beigi NMA, Broumandfar K, Bahadoran P, et al. Women's experience of pain during childbirth. *Iran J Nurs Midwifery Res* 2010;15:77–82.

3. Devilata T, Swarna S. Effectiveness of pre delivery preparation on anxiety among Primigravida mothers at maternal child health centre Tirupati, AP, India. *IOSR J Nurs Heal Sci* 2015;4:19-24. https://doi.10.9790/1959-04651924.

4. Aksoy M, Aksoy AN, Dostbil A, et al. The Relationship between Fear of Childbirth and Women ' s Knowledge about Painless Childbirth. *Obstet Gynecol Int* 2014;2014:7. http://dx.doi.org/10.1155/2014/274303

5. Nystedt A, Hildingsson I. Diverse definitions of prolonged labour and its consequences with sometimes subsequent inappropriate treatment. *BMC Pregnancy Childbirth* 2014;14:233. https://doi.org/10.1186/1471-2393-14-233

6. Hanjani SM, Tourzani ZM, Shoghi M. The Effect of Foot Reflexology on Anxiety , Pain , and Outcomes of the Labor in Primigravida Women. Acta Med Iran. 2014;53:507–511.

7. Li W, Zhang H, Ling Y, et al. Effect of prolonged second stage of labor on maternal and neonatal outcomes. *Asian Pac J Trop Med* 2011;4:409–411. https://doi.org/10.1016/S1995-7645(11)60114-4

8. Neal JL, Lamp JM, Buck JS, et al. Outcomes of Nulliparous Women with Spontaneous Labor Onset Admitted to Hospitals in Pre-active versus Active Labor. *J Midwifery Womens Heal* 2014;59:28–34. doi:10.1111/jmwh.12160.Outcomes

9. Kjærgaard H, Olsen JØRN, Ottesen B, et al. Incidence and outcomes of dystocia in the active phase of labor in term nulliparous women with spontaneous labor onset. *Acta Obstet Gynecol* 2009;88:402-407. doi:10.1080/00016340902811001

10. Lowe NK. A Review of Factors Associated With Dystocia and Cesarean Section in Nulliparous Women. *J Midwifery Women's Heal* 2007;52:216–228. doi:10.1016/j.jmwh.2007.03.003

11. Shields SG, Ratcliffe SD, Fontaine P, et al. Dystocia in nulliparous women. *Am Fam Physician* 2007;75:1671-1678.

12. Garthus-Niegel S, Knoph C, von Soest T, et al. The Role of Labor Pain and Overall Birth Experience in the Development of Posttraumatic Stress Symptoms: A Longitudinal Cohort Study. *Birth* 2014;41:108–115. https://doi.org/10.1111/birt.12093

13. Peeler S, Stedmon J, Chung MC, et al. Women's experiences of living with postnatal PTSD. *Midwifery* 2018;56:70–78. https://doi.org/10.1016/j.midw.2017.09.019

14. Boryri T, Noori NM, Teimouri A, et al. The perception of primiparous mothers of comfortable resources in labor pain (a qualitative study). *Iran J Nurs Midwifery Res* 2016;21:239–246. https:// doi.org/10.4103/1735-9066.180386

15. Størksen HT, Garthus-niegel S, Adams SS, et al. Fear of childbirth and elective caesarean section : a population-based study. *BMC Pregnancy Childbirth* 2015;15:221. https://doi.org/10.1186/s12884-015-0655-4

16. Stoll KH, Hauck YL, Downe S, et al. Preference for cesarean section in young nulligravid women in eight OECD countries and implications for reproductive health education. *Reprod Health* 2017;14:116. https://doi.org/10.1186/s12978-017-0354-x

17. El-Aziz SNA, Mansour SE, Hassan NF. Factors associated with fear of childbirth: It's effect on women's preference for elective cesarean section. *J Nurs Educ Pract* 2017;7:133–45. https://doi.org/10.5430/jnep.v7n1p133.

18. Lowe NK. The Pain and Discomfort of Labor and Birth. *J Obstet Gynecol Neonatal Nurs* 1996;25:82–92. https://doi.org/10.1111/j.1552-6909.1996.tb02517.x

19. Rayburn WF, Zuspan FP. Drug therapy in obstetrics and gynecology. 3rd ed. St. Louis:Mosby; 1992. Book

20. Ullman R, Smith LA, Burns E, et al. Parenteral opioids for maternal pain management in labour. Cochrane Database *Syst Rev* 2010;9. https://doi.org/10.1002/14651858.CD007396.pub2

21. Pereira RR, Kanhai H, Rosendaal F, et al. Parenteral Pethidine for labour pain relief and substance use disorder : 20-year follow-up cohort study in offspring. *BMJ Open* 2012;2:e000719. http://dx.doi.org/10.1136/bmjopen-2011-000719

22. Smith LA, Burns E, Cuthbert A. Parenteral opioids for maternal pain management in labour. Cochrane Database *Syst Rev* 2018;6. https://doi.org/10.1002/14651858.CD007396.pub3

23. Simkin P. Reducing Pain and Enhancing Progress in labor : A Guide to Nonpharmacologic Methods for Maternity Caregivers. *Birth* 1995;22:161–71. https://doi.org/10.1111/j.1523-536X.1995.tb00693.x

24. Cook A, Wilcox G. Pressuring Pain: Alternative Therap for Labor Pain Management. AWHONN *Lifelines* 1997;1:36–41. https://doi.org/10.1111/j.1552-6356.1997.tb00929.x

25. Jones LV. Non-pharmacological approaches for pain relief during labour can improve maternal satisfaction with childbirth and reduce obstetric interventions. *Evid Based Nurs* 2015;18:70. http://dx.doi.org/10.1136/eb-2014-101938

26. Busch V, Magerl W, Kern U, et al. The Effect of Deep and Slow Breathing on Pain Perception , Autonomic Activity , and Mood Processing -An Experimental Study. *Pain Med* 2012;13:215–28. https://doi.org/10.1111/j.1526-4637.2011.01243.x

27. Thomas ME, Dhiwar MS. Effectiveness of Patterned Breathing Technique in Reduction of Pain During First Stage of Labour Among Primigravidas. Sinhgad E-*Journal Nurs* 2011;1:6–8.

28. Kaur K, Rana AK, Gainder S. Effect of video on ' Breathing Exercises during labour ' on Pain Perception and Duration of Labour Among Primigravida Mothers. *Nurs Midwifery Res Journa* 2013;9:1–9.

29. El-refaye GE, El Nahas EM, Ghareeb HO. Effect of kinesio taping therapy combined with breathing exercises on childbirth duration and labor pain : a randomized controlled trial. *Bull Fac Phys Ther* 2016;21:23–31. https:// doi.10.4103/1110-6611.188026

30. Chuang LL, Lin LC, Cheng P, et al. Effects of a relaxation training programme on immediate and prolonged stress responses in women with preterm labour. *J Adv Nurs* 2011;68:170–80. https://doi.org/10.1111/j.1365-2648.2011.05765.x

31. Akbarzadeh M, Sharif F, Zare N. The Reduction of Anxiety and Improved Maternal Attachment to Fetuses and Neonates by Relaxation Training in Primigravida Women. *Women's Heal Bull* 2014;1:e18968. https://doi.org/10.17795/whb-18968.

32. Nattah FM, Abbas WAK. Assessment of Level of Pain and its Relation with Breathing Exercise in the First Stage of Labour among Primi Mothers at Hilla Teaching Hospital. *Eur J Sci Res* 2016;135:121–8.

33. Yuksel H, Cayir Y, Kosan Z, et al. Effectiveness of breathing exercises during the second stage of labor on labor pain and duration : a randomized controlled trial. *J Integr Med* 2017;15:456–61. https://doi.org/10.1016/S2095-4964(17)60368-6

34. Mathew AM, Francis F. Effectiveness of Foot Refl exology in Reduction of Labour Pain among Mothers in Labour Admitted at PSG Hospital, Coimbatore. *Int J Nurs Educ* 2016;8:11–5. https://doi.org/10.5958/0974-9357.2016.00081.7

35. Moghimi-Hanjani S, Mehdizadeh-Tourzani Z, Shoghi, M. The effect of foot reflexology on anxiety, pain, and outcomes of the labor in primigravida women. *Acta Med Iran* 2015;53:507–511.

36. Cohen M. The Effectiveness of Massage Therapy A Summary of Evidence-Based Research. Melbourne:Australian Associaiton of Massage Therapy;2011.

37. Dolatian M, Hasanpour A, Montazeri S, et al. The effect of reflexology on pain intensity and duration of labor on primiparas. *Iran Red Crescent Med J* 2011;13:475–479.

38. Valiani M, Shiran E, Kianpour M, et al. Reviewing the effect of reflexology on the pain

and certain features and outcomes of the labor on the primiparous women. *Iran J Nurs Midwifery Res* 2010;15:302–310.

39. Baljon K, Romli MH, Ismail AH, et al. The Effectiveness Of Complementary And Alternative Medicine Of Massage And Reflexology In Managing Pain And Anxiety Among Primigravidas In Labor: A Systematic Review.[in preparation for submission to a journal]

40. Field T, Hernandez-Rief M, Diego M, et al. Cortisol decreases and serotonin increases following massage therapy. *J Neurosci* 2005;115:1397–413. https://doi.org/10.1080/00207450590956459

41. Crowe K, von Baeyer C. Predictors of a Positive Childbirth Experience. *Birth Iss Perinat C* 1989;16:59–63. https://doi.org/10.1111/j.1523-536X.1989.tb00862.x

42. Ma X, Yue ZQ, Gong ZQ, et al. The effect of diaphragmatic breathing on attention, negative affect and stress in healthy adults. *Front Psychol* 2017;8:1–12. https://doi.org/10.3389/fpsyg.2017.00874

43. Bordoni B, Purgol S, Bizzarri A, et al. The Influence of Breathing on the Central Nervous System. *Cureus* 2018;10:1–8. https://doi.org/10.7759/cureus.2724

44. McCullough JE, Close C, Liddle SD et al. A pilot randomised controlled trial exploring the effects of antenatal reflexology on labour outcomes. *Midwifery*, 2017;55: 137–144.

45. Mathew AM, Francis F. Effectiveness of Foot Reflexology in Reduction of Labour Pain among Mothers in Labour Admitted at PSG Hospital, Coimbatore. *Int J Nurs Educ* 2016;8:11–15.

46. Embong NH, Soh YC, Ming LC, et al. Revisiting reflexology: Concept, evidence, current practice, and practitioner training. *J Tradit Complement Altern Med* 2015;5:197–206.

47. Tiran D, Chummun H. The physiological basis of reflexology and its use as a potential diagnostic tool. *Complement Ther Clin Pract* 2005;11:58–64. https://doi.org/10.1016/j.ctnm.2004.07.007

48. Levy I, Attias S, Lavee TS, et al. The effectiveness of foot reflexology in reducing anxiety and duration of labor in primiparas: An open-label randomized controlled trial. *Complement Ther Clin Pract* 2020;38:101085. https://doi.org/10.1016/j.ctcp.2019.101085

49. Yılar Erkek Z, Aktas S. The effect of foot reflexology on the anxiety levels of women in labor. *J Altern Complement Med Medicine*, 2018;24:352–360. https://doi.org/10.1089/acm.2017.0263

50. Tiran D, Chummun H. The physiological basis of reflexology and its use as a potential

diagnostic tool. *Complement Ther Clin Pract* 2005;11:58–64. https://doi.org/10.1016/j.ctnm.2004.07.007.

51. Tappan FM, Benjamin PJ. Tappan's handbook for healing massage techniques. Classic, Holistic, and Emerging Methods. 3rd Ed. Stamford, Conn.: Appleton & Lange.; 1998.

52. Tiran D, Evans M. Theoretical background to structural reflex zone therapy. *Pract Manag Pain*; 2010.

53. Embong NH, Soh YC, Ming LC, et al. Revisiting reflexology: Concept, evidence, current practice, and practitioner training. *J Tradit Complement Med* 2015;5:197–206. https://doi.org/10.1016/j.jtcme.2015.08.008

54. Poole H, Glenn S, Murphy P. A randomised controlled study of reflexology for the management of chronic low back pain. *Eur J Pain* 2007;11:878–87. https://doi.org/10.1016/j.ejpain.2007.01.006

55. Keet L. Reflexology Bible: The Definitive Guide to Reflexology (Godsfield Bible Series). First Edit. London,Great Britain: Octopus publishing group; 2008. Book

56. Roudaut Y, Lonigro A, Coste B, et al. Touch sense: functional organization and molecular determinants of mechanosensitive receptors. *Channels* 2012;6:234–45. https://doi.org/10.4161/chan.22213

57. Goats GC. Massage--the scientific basis of an ancient art: Part 2. Physiological and therapeutic effects. *Br J Sports Med* 1994;28:153–6. http://dx.doi.org/10.1136/bjsm.28.3.153

58. Basbaum AI, Fields HL. Endogenous pain control mechanisms: Review and hypothesis. *Ann Neurol* 1978;4:451–62. http://dx.doi.org/10.1002/ana.410040511

59. Weerapong P, Hume PA, Kolt GS. The mechanisms of massage and effects on performance, muscle recovery and injury prevention. *Sport Med* 2005;35:235–56. http://dx.doi.org/10.2165/00007256-200535030-00004

60. Vakilian K, Keramat A. The Effect of the Breathing Technique With and Without Aromatherapy on the Length of the Active Phase and Second Stage of Labor. *Nurs Midwifery Stud* 2013;2. http://dx.doi.org/10.5812/nms.9886

61. Morhenn V, Beavin LE, Zak PJ. Massage Increases Oxytocin and Reduces Adrenocorticotropin Hormone in Humans. *Altern Ther* 2012;18:11–8.

62. Diego MA, Field T. Moderate Pressure Massage Elicits a Parasympathetic Nervous System Response. *Int J Neurosci* 2009;119:630–8. http://dx.doi.org/10.1080/00207450802329605

63. McCullough JE, Liddle SD, Sinclair M, et al. The Physiological and Biochemical Outcomes Associated with a Reflexology Treatment : A Systematic Review. Evidence-

Based Complementary *Altern Med* 2014;2014. http://dx.doi.org/10.1155/2014/502123

64. Mccullough JEM, Liddle SD, Close C, et al. Reflexology: a randomised controlled trial investigating the effects on beta-endorphin, cortisol and pregnancy related stress. *Complement Ther Clin Pract* 2018; 31:76–84.

65. Li Q, Becker B, Wernicke J, et al. Foot massage evokes oxytocin release and activation of orbitofrontal cortex and superior temporal sulcus. *Psychoneuroendocrinology* 2018;101:193–203. http://dx.doi.org/10.1016/j.psyneuen.2018.11.016

66. Bell AF, Erickson EN, Carter CS. Beyond Labor: The Role of Natural and Synthetic Oxytocin in The Transition To Motherhood. *J Midwifery Womens Hea*l 2015;59:35–42. http://dx.doi.org/10.1111/jmwh.12101

67. Hu J, Brettle A, Jiang Z, et al. A systematic review and meta-analysis of the effect of massage therapy in pain relief during labor. *J Nurs* 2017;6:1–14. http://dx.doi.org/10.18686/jn.v6i4.130

68. Huntley AL, Coon JT, Ernst E. Complementary and alternative medicine for labor pain : A systematic review. *Am J Obstet Gynecol* 2004;191:36–44. http://dx.doi.org 10.1016/j.ajog.2003.12.008

69. Ranjbaran M, Khorsandi M, Matourypour P, et al. Effect of Massage Therapy on Labor Pain Reduction in Primiparous Women A Systematic Review and Meta-analysis of Randomized Controlled Clinical Trials in Iran. *Iran J Nurs Midwifery Res* 2017;22:257–61.

70. Smith CA, Levett KM, Collins CT, et al. Massage , reflexology and other manual methods for pain management in labour (Review). *Cochrane Database Rev*. 2012. (2018)

71. Kirkham M. The Midwife-Mother Relationship. 2nd ed. Hampshire: Red Globe Press; 2000. book

72. Levett KM, Smith CA, Bensoussan A, et al. The Complementary Therapies for Labour and Birth Study: Making sense of labour and birth – experiences of women, partners and midwives of a complementary medicine antenatal education course. *Midwifery* 2016;40:124–131. http://dx.doi.org/10.1016/j.midw.2016.06.011

73. Ministry of Health Saudi Arabia. Maternity and Children Hospital Makkah. 2013. http://www.testonserver.com/mch/ (accessed November 27, 2018).

74. Altaweli RF, McCourt C, Baron M. Childbirth care practices in public sector facilities in Jeddah, Saudi Arabia: A descriptive study. *Midwifey* 2014;30:899–909. http://dx.doi.org/10.1016/j.midw.2014.03.006

75. Farine D, Seaward PG. When it comes to pregnant women sleeping, is left right? *J Obstet Gynaecol Can* 2007;*29*:841–842.

76. Bonnel AM, Boureau F. Labor Pain Assessment : Validity of a Behavioral Index. *Pain* 1985;22:81–90. https://doi.org/10.1016/0304-3959(85)90150-2

77. Chang M, Wang S, Chen C. Effects of massage on pain and anxiety during labour : a randomized controlled trial in Taiwan. *J Adv Nurs* 2002;38:68-73.

78. Mårtensson L, Bergh I. Effect of treatment for labor pain : Verbal reports versus visual analogue scale scores - A prospective randomized study. *Int J Nurs Midwifery* 2011;3:43–7.

79. Bahammam MA, Hassan MH. Validity and reliability of an Arabic version of the modified dental anxiety scale in Saudi adults. *Saudi Med J* 2014;35:1384. http://dx.doi.org/10.2466/pr0.1997.80.3.947

80. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: Visual analog scale for pain (vas pain), numeric rating scale for pain (nrs pain), mcgill pain questionnaire (mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap). *Arthritis Care Res* 2011;63:S240-S252. doi:10.1002/acr.20543

81. Taghinejad H, Delpisheh A, Suhrabi Z. Comparison between massage and music therapies to relieve the severity of labor pain. *Womens Health* 2010;6:377–381. https://doi.org/10.2217/WHE.10.15

82. Jensen MP, Karoly P, Braver S. The Measurement of Clinical Pain Intensity : a Comparison of Six Methods. *Pain Res Manag* 1986;27:117–26. https://doi.org/10.1016/0304-3959(86)90228-9

83. Durat G, Çulhacik GD, Doğu Ö, et al. The development of an anxiety assessment scale for pregnant women in labor. *Saudi Med J* 2018;39:609–14. http://dx.doi.org/10.15537/smj.2018.6.22266

84. Wei CK, Leng CY, Lin SKS. The use of the Visual Analogue Scale for the assessment of labour pain: a systematic review. *JBI Database Syst Rev Implement* 2010;8:972–1015

85. Harvey S, Rach D, Stainton MC, et al. Evaluation of satisfaction with midwifery care.*Midwifery* 2002;18:260–267. http://dx.doi.org/10.1054/midw.2002.0317

86. Bublitz MH, Bourjeily G, D'Angelo C, et al. Maternal sleep quality and diurnal cortisol regulation over pregnancy. *Behav Sleep Med* 2018;16:282–293. https://doi.org/10.1080/15402002.2016.1210147

87. Larsson CA, Gullberg B, Råstam L, et al. Salivary cortisol differs with age and sex and shows inverse associations with WHR in Swedish women: a cross-sectional study. *BMC endocr disord* 2009;*9*:16.

88. Sundaram, L., Swaminathan, S., Ranjakumar, T., Ashraf, R., & Das, T. K. (2017). Intraocular pressure variation in pregnancy: a prospective study. *Int J Reprod Contracept Obstet Gynecol*, *5*, 1406–1409. http://dx.doi.org/10.18203/2320-1770.ijrcog20161294

89. Romano A, Tempesta B, Micioni Di Bonaventura MV. et al. From autism to eating disorders and more: the role of oxytocin in neuropsychiatric disorders. *Fron Neurosci* 2016;9:497. https://doi.org/10.3389/fnins.2015.00497

90. Uvnäs-Moberg K, Ekström-Bergström A, Berg M. et al. Maternal plasma levels of oxytocin during physiological childbirth–a systematic review with implications for uterine contractions and central actions of oxytocin. *BMC Pregnancy Childb* 2009;19:285.

91. Snyder M, Wieland J. Complementary and alternative therapies : what is their place in the management of chronic pain ? *Nurs Clin North Am* 2003;38:495–508. http://dx.doi.org/10.1016/S0029-6465(02)00098-1

92. Sekhavat L, Behdad S. The effects of meperidine analgesia during labor on fetal heart rate. *Int J Biomed Sci* 2009;5:59.

93. Reynolds F. The effects of maternal labour analgesia on the fetus. *Best Pract Res Clin Obstet Gynaecol* 2010;24:289–302. https://doi.org/10.1016/j.bpobgyn.2009.11.003

94. Whitburn LY, Jones LE, Davey M, et al. The nature of labour pain : An updated review of the literature. *Women and Birth* 2018;32:28-38. http://dx.doi.org/10.1016/j.wombi.2018.03.004

95. Woo AK. Depression and Anxiety in Pain. *Br J Pain* 2010;4:8–12. https://doi.org/10.1177/204946371000400103

96. Turner, J. A., Deyo, R. A., Loeser, J. D., Von Korff, M., & Fordyce, W. E. (1994). The importance of placebo effects in pain treatment and research. *J Am Med Assoc* 1994;*271*:1609–1614. https://doi.org/10.1001/jama.1994.03510440069036

97. Brook CA, Schmidt LA. Social anxiety disorder: A review of environmental risk factors. *Neuropsychiatr Dis Treat* 2008;4:123–43.

Figure Legend

Figure 1 Mechanisms of action Reflexology therapy.

Figure 2 Mechanisms of action Massage therapy.

Figure 3 CONSORT flow diagram.

Figure 4 Research personnel training and responsibility matrix.

Figure 5 (a) shows the timeline of outcomes measurement in the intervention group; (b) shows the timeline of outcomes measurement in the control group.

Table Legend

Table 1 Steps of the Intervention.

Table 2 Summary of Primary Outcomes and Measurement Tools.

Table 3 Summary of Secondary Outcomes and Measurement Tools.

Table 1: Steps of the Intervention

Steps	Process
1.	Prepare the equipment.
2.	Explain the procedure to the primigravida & advise her to lay on her left side* with a pillow on the side of her stomach.
Breathing Exercise Intervention for 5 minutes	
3.	Ask the primigravida to perform deep breathing by inhaling slowly through the nose for two seconds and then consciously release the air by breathing out for another two seconds during contractions.
4.	Rest for 1–3 seconds, then repeat the same technique for a total of 5 minutes. Then proceed to the reflexology as described below.
Reflexology Intervention Technique for 10 minutes on each foot	
5.	Put a towel under the right foot and cover the left leg.
6.	Apply warm oil over the right foot and roll it left to right 5 times.
7.	Press palms on the Achilles heel and knead the ankle 5 times.
8.	Knead the thumb pads on the central and bottom parts of the heel 5 times.
9.	Knead the foot following the CIUW** shape on the lateral and intermediate aspects of the foot followed by the MST*** shape 5 times.
10.	Press the wooden reflexology stick on the toes, forefoot, mid-foot, and hind-foot 5 times.
11.	Repeat Steps 5–11 on the opposite side. Then proceed to the next lower limbs massage.
Lower Limbs Massage for 2 minutes 30 seconds on each leg	
12.	Effleurage massage on the whole, lower flexed leg by using two hands 3 times.
13.	Half effleurage massage from the heel to the popliteal area 3 times.
14.	Palm and thumb kneading on the gastrocnemius muscle over the lateral & medial sides, followed by scooping on the gastrocnemius, each step 3 times.
15.	Thumb kneading on the hamstring muscle over the medial, intermediate, and lateral sides 3 times.
16.	Repeat Steps 12–17 on the right leg. Then proceed to lower back massage.
Lower Back Massage for 15 minutes	
17.	Effleurage massage from the sacrum to the shoulders and deltoids 3 times.
18.	Thumb kneading & pressure over the lateral sides of the lumbar area of the spine 3 times.
19.	Apply fist knuckling motion and thumb kneading on the lower back, side by side, 3 times. Then proceed to upper back massage.

Upper Back Massage for 15 minutes	
20.	Effleurage massage followed by palm kneading from the lumbar region to trapezius laterally 3 times.
21.	Thumb kneading over both sides of erector spinae, then draining between the ribs towards the armpit areas 3 times.
22.	Apply squeeze on the deltoid muscle with draining towards the armpit 3 times.
23.	Apply finger kneading on trapezius muscle, followed by fist scooping 3 times.
24.	Finally, press on the neck and shoulder area on both sides 3 times.

* The left side position allows maximum blood flow to the placenta, because it applies less pressure from the foetus on the vena cava [75].

**CIUW shape: C-shape; I-shape; U-shape, and W-shape. These shapes indicate the orientation and placement of the palms and knuckles of the therapist.

***MST shape: M-shape, S-shape, and T-shape. These shapes indicate the orientation and placement of the palms and knuckles of the therapist.

Table 2: Summary of Primary Outcomes and Measurement Tools

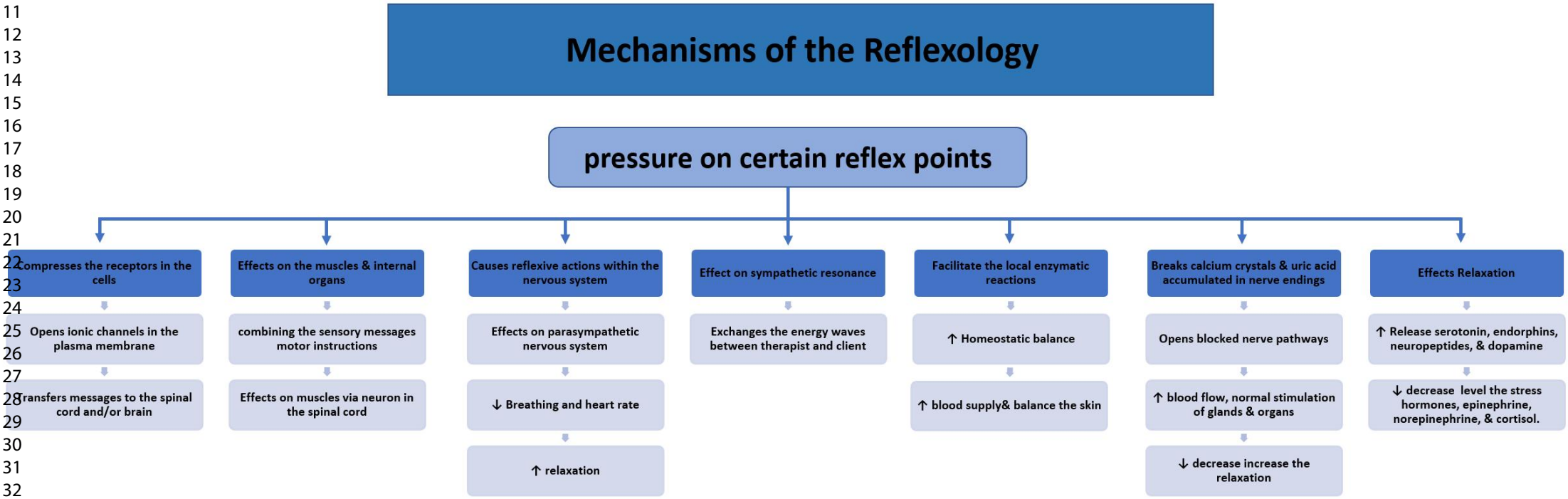
Primary Outcomes	Tools	Psychometric tests	Method of assessment
Pain	PBI	100% inter-rater reliability *r* coefficient was 0.45, 0.50, and 0.44 between PBI and PPI [76, 77].	Assessor-rated [76], five-category behavioural observation scale
	VAS	Moderate correlation ($r = 0.54$) with the verbal rating and is considered valuable when mixed with other tools [78, 79]; 0.97 intraclass correlation coefficient of 24 hours interval test-retest reliability [80].	Self-reported VAS [81], contains six different coloured parts anchored by two extremes of 'no pain' and excruciating pain to mark on the line-map by primigravidae [82].
Anxiety	AASPWL	> 0.8 concordance test content validity index Kendall's W between the opinions of the experts (W= 0.090; *P*= 0.080) with Cronbach's alpha level of 0.77 [83]; significantly correlated (*r*= 0.369) with the Beck Anxiety Scale [83].	Questionnaire consists of nine items [83], on a 5-point scale: the higher the mean score the higher the anxiety

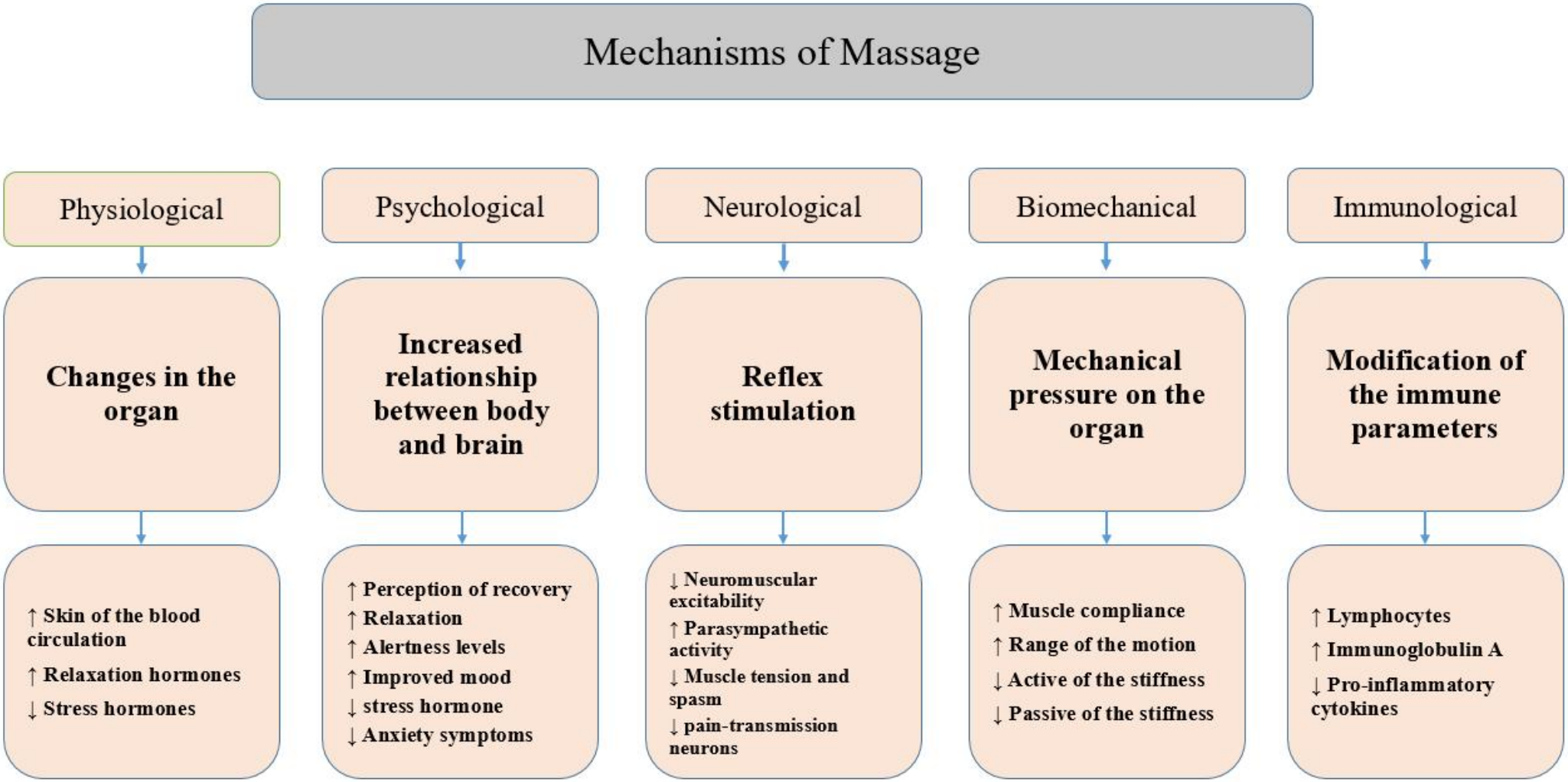
PBI= Present Behavioural Intensity; VAS= Visual Analog Scale; AASPWL= Anxiety Assessment Scale for Pregnant Women in Labour.

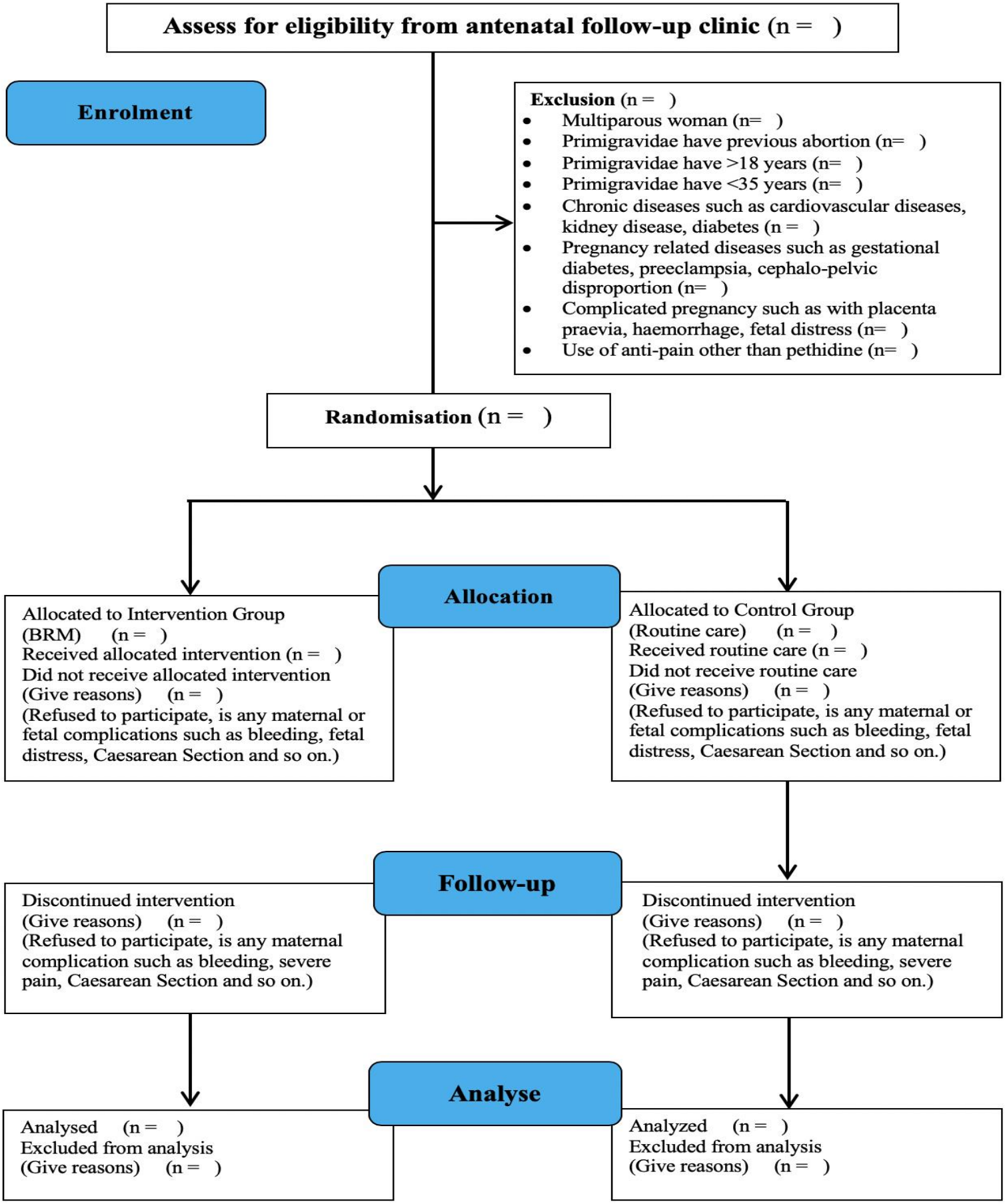
Table 3 Summary of Secondary Outcomes and Measurement Tools

Secondary outcomes	Measurement tools	Method of assessment
Maternal stress hormones level	Blood sample for ACTH, cortisol, oxytocin	Blood sample will be drawn from the median cubital vein during the insertion of IV cannula (routine care)
Maternal vital sign	Thermometer Sphygmomanometer	Recorded on the vital sign monitoring chart and cardiotocograph.
FHR	Cardiotocograph	Recorded on the vital sign monitoring chart, cardiotocograph chart, and partograph.
Duration of labour	Partograph	Partograph at two separate time intervals, a sum of labour duration from 3 to 6 cm of cervical dilatation and from 6 cm to delivery of the placenta
Neonatal Apgar score	Apgar score table	Taken from the delivery room medical record
Maternal satisfaction	Six Simple Questions [85].	Self-reported 7-point scale (1-7) from "strongly disagree to "strongly agree" with higher scores signifying the higher level of satisfaction

ACTH= adrenocorticotropic hormone


Mechanisms of the Reflexology
pressure on certain reflex points
Compresses the receptors in the cells
Opens ionic channels in the plasma membrane
Transfers messages to the spinal cord and/or brain
Effects on the muscles & internal organs
combining the sensory messages motor instructions
Effects on muscles via neuron in the spinal cord
Causes reflexive actions within the nervous system
Effects on parasympathetic nervous system
↓ Breathing and heart rate
↑ relaxation
Effect on sympathetic resonance
Exchanges the energy waves between therapist and client
Facilitate the local enzymatic reactions
↑ Homeostatic balance
↑ blood supply& balance the skin
Breaks calcium crystals & uric acid accumulated in nerve endings
Opens blocked nerve pathways
↑ blood flow, normal stimulation of glands & organs
↓ decrease increase the relaxation
Effects Relaxation
↑ Release serotonin, endorphins, neuropeptides, & dopamine
↓ decrease level the stress hormones, epinephrine, norepinephrine, & cortisol.


Mechanisms of Massage
Physiological
Psychological
Neurological
Biomechanical
Immunological
Changes in the organ
Increased relationship between body and brain
Reflex stimulation
Mechanical pressure on the organ
Modification of the immune parameters
↑ Skin of the blood circulation
↑ Relaxation hormones
↓ Stress hormones
↑ Perception of recovery
↑ Relaxation
↑ Alertness levels
↑ Improved mood
↓ stress hormone
↓ Anxiety symptoms
↓ Neuromuscular excitability
↑ Parasympathetic activity
↓ Muscle tension and spasm
↓ pain-transmission neurons
↑ Muscle compliance
↑ Range of the motion
↓ Active of the stiffness
↓ Passive of the stiffness
↑ Lymphocytes
↑ Immunoglobulin A
↓ Pro-inflammatory cytokines


Assess for eligibility from antenatal follow-up clinic (n =)
Enrolment
Exclusion (n =)
Multiparous woman (n=)
Primigravidae have previous abortion (n=)
Primigravidae have >18 years (n=)
Primigravidae have <35 years (n=)
Chronic diseases such as cardiovascular diseases, kidney disease, diabetes (n =)
Pregnancy related diseases such as gestational diabetes, preeclampsia, cephalo-pelvic disproportion (n=)
Complicated pregnancy such as with placenta praevia, haemorrhage, fetal distress (n=)
Use of anti-pain other than pethidine (n=)
Randomisation (n =)
Allocation
Allocated to Intervention Group (BRM) (n =)
Received allocated intervention (n =)
Did not receive allocated intervention (Give reasons) (n =)
(Refused to participate, is any maternal or fetal complications such as bleeding, fetal distress, Caesarean Section and so on.)
Allocated to Control Group (Routine care) (n =)
Received routine care (n =)
Did not receive routine care (Give reasons) (n =)
(Refused to participate, is any maternal or fetal complications such as bleeding, fetal distress, Caesarean Section and so on.)
Follow-up
Discontinued intervention (Give reasons) (n =)
(Refused to participate, is any maternal complication such as bleeding, severe pain, Caesarean Section and so on.)
Discontinued intervention (Give reasons) (n =)
(Refused to participate, is any maternal complication such as bleeding, severe pain, Caesarean Section and so on.)
Analyse
Analysed (n =)
Excluded from analysis (Give reasons) (n =)
Analyzed (n =)
Excluded from analysis (Give reasons) (n =)

13 Research Assistants + 1 Principal Investigator

- Recruitment of nursing students who completed a 5-year nursing degree training and awaiting their job posting.
- Assigned to their preferred and suitable roles (coordinators, the outcome assessors, or massage therapists).
- One week training as research assistants in their respective roles.
- A pilot study to ensure their competency.
- Written study manual as a reference guide to be provided to all research assistants.

Research coordinators (4 pax.)	Outcome Assessors (4 pax.)	Massage therapists (5 pax.)
• Recruit eligible primigravidae at the antenatal clinic deliver brief health education on labour pain management at the antenatal clinic for 6 weeks. • Reassess the primigravidae women's consent and eligibility, • Allocate the women to either the intervention or control group. • Alert the massage therapists and outcome assessors when the cervical dilatation of the trial participant reaches 6 cm. • Distribute outcomes assessment record form to the outcome assessors. • Encode the questionnaire package according to the participant's allocated group. • Organise the entry sequence for the outcome assessors and the massage therapists to enter the delivery rooms according to the scheduled time.	• Assess and fill-up questionnaires: 1. Present behavioural Intensity (PBI). 2. Visual Analog Scale (VAS). 3. Anxiety Assessment Scale for primigravidae Women in labour (AASPWL), 4. Six Simple Questions (SSQ) for maternal satisfaction. • Retrieve the maternal vital signs, fetal heart rate, duration of labour, and neonatal Apgar score from the health records. • Record all the outcomes in the designated form.	• Perform breathing exercise, foot reflexology and back massage during labour (BRM). 1. Breathing exercise (5min). 2. Foot Reflexology (10 min on each foot), 3. Back massage (35min).

Sub-divided into two shifts per day to ensure all the eligible and consented primigravidae will be captured

Day Shift (9 am - 9pm)

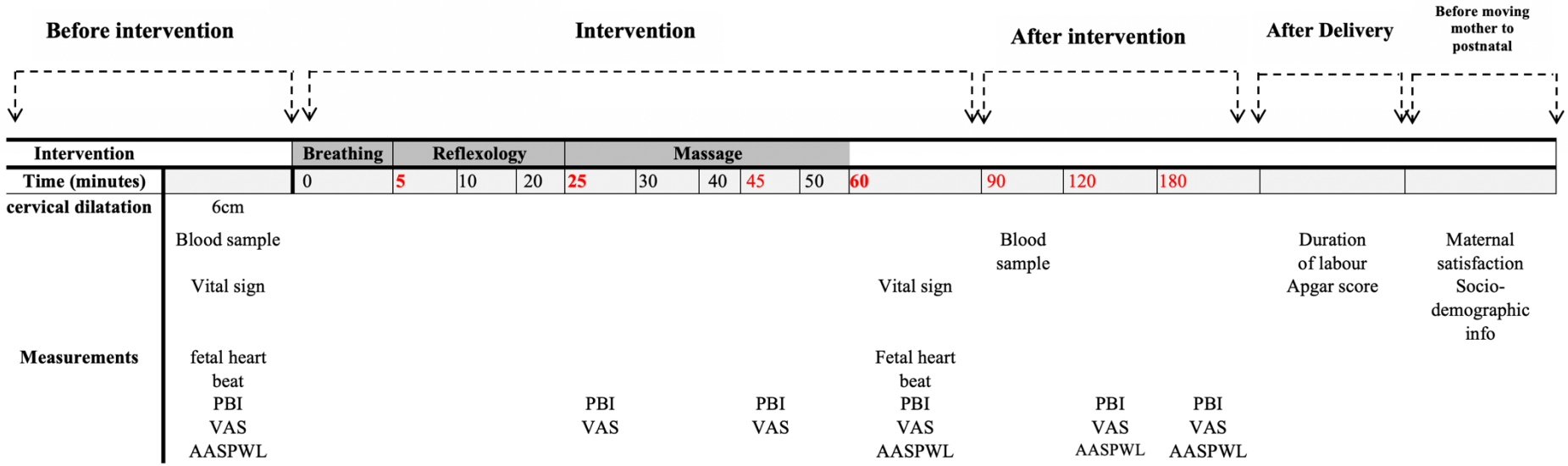
2 Coordinators, 3 Massage therapists, and 2 Outcome Assessors

Night Shift (9 pm - 9 am)

2 Coordinators, 2 Massage therapists, 2 Outcome Assessors, and Principal Investigator

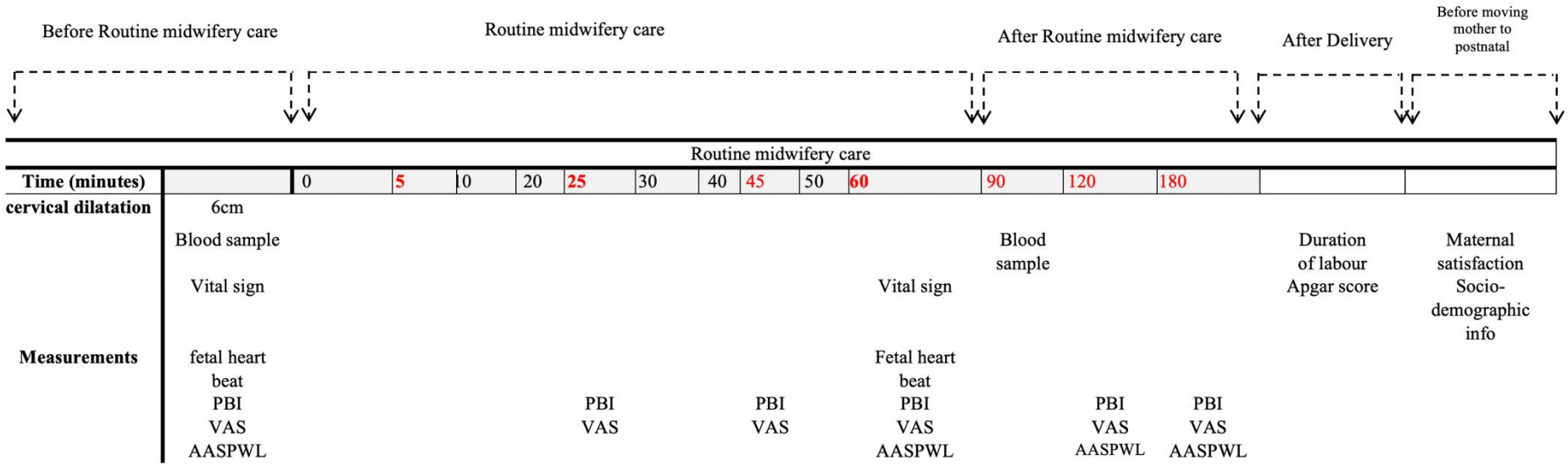
a

Intervention Group



b

Control Group



BMJ Open

Effectiveness of Breathing Exercises, Foot Reflexology and Back Massage (BRM) on Labour Pain, Anxiety, Duration, Satisfaction, Stress Hormones, and New-born Outcomes among Primigravidae during the First Stage of Labour in Saudi Arabia: A Study Protocol for a Randomised Controlled Trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-033844.R2
Article Type:	Protocol
Date Submitted by the Author:	14-Apr-2020
Complete List of Authors:	Baljon, Kamilya; Universiti Putra Malaysia Faculty of Medicine and Health Sciences, Department of Family Medicine; Umm Al-Qura University, Department of Nursing Romli, Muhammad Hibatullah ; Universiti Putra Malaysia Faculty of Medicine and Health Sciences, Department of Nursing & Rehabilitation Ismail @ Daud, Adibah Hanim; Universiti Putra Malaysia Faculty of Medicine and Health Sciences, Department of Family Medicine Khuan, Lee; Universiti Putra Malaysia Faculty of Medicine and Health Sciences, Department of Nursing & Rehabilitation Chew, Boon; Universiti Putra Malaysia Faculty of Medicine and Health Sciences, Department of Family Medicine
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Complementary medicine, Nursing, Emergency medicine, General practice / Family practice, Public health
Keywords:	Breathing exercises, Reflexology, Massage, Primigravidae, Labour pain, Stress hormones

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Effectiveness of Breathing Exercises, Foot Reflexology and Back Massage (BRM) on Labour Pain, Anxiety, Duration, Satisfaction, Stress Hormones and New-born Outcomes among Primigravidae during the First Stage of Labour in Saudi Arabia: A Study Protocol for a Randomised Controlled Trial

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ABSTRACT

Introduction Labour pain is among the severest pains primigravidae may experience during pregnancy. Failure to address labour pain and anxiety may lead to abnormal labour. Despite the many complementary non-pharmacological approaches to coping with labour pain, the quality of evidence is low and best approaches are not established. This study protocol describes a proposed investigation of the effects of a combination of breathing exercises, foot reflexology and back massage (BRM) on the labour experiences of primigravidae.

Methods and analysis This randomised controlled trial will involve an intervention group receiving BRM and standard labour care, and a control group receiving only standard labour care. Primigravidae of 26–34 weeks of gestation without chronic diseases or pregnancy-related complications will be recruited from antenatal clinics. Eligible and consenting patients will be randomly allocated to the intervention or the control group stratified by intramuscular pethidine (IMP) use. The BRM intervention will be delivered by a trained massage therapist. The primary outcomes of labour pain and anxiety will be measured during and after uterine contractions at baseline (cervical dilatation 6 cm) and post-BRM hourly for two hours. The secondary outcomes include maternal stress hormone (adrenocorticotropic hormone, cortisol and oxytocin) levels, maternal vital signs (V/S), foetal heart rate (FHR), labour duration, Apgar scores, and maternal satisfaction. The sample size is estimated based on the between-group difference of 0.6 in anxiety scores, 95% power and 5% α error, which yields a required sample size of 154 (77 in each group) accounting for a 20% attrition rate. The between- and within-group outcome measures will

be examined with mixed-effects regression models, time series analyses and paired t-test or equivalent non-parametric tests, respectively.

Ethics and dissemination Ethical approval was obtained from the Ethical Committee for Research Involving Human Subjects of the Ministry of Health in the Saudi Arabia (H-02-K-076-0319-109) on 14 April 2019, and from the Ethics Committee for Research Involving Human Subjects (JKEUPM) Universiti Putra Malaysia on 23 October 2019, reference number: JKEUPM-2019-169. Written informed consent will be obtained from all participants. Results from this trial will be presented at regional, national and international conferences and published in indexed journals.

Trial registration number and date ISRCTN87414969, registered 3 May 2019

Keywords Breathing exercises, Reflexology, Massage, Primigravidae, Labour pain, Stress hormones.

Article Summary

Strengths and Limitations of the Study

- This single-blind, parallel, randomised controlled trial will explore the combined effects of breathing exercises, foot reflexology and back massage (BRM) on pain and anxiety during labour in healthy primigravidae with a singleton foetus.
- The effects of BRM will also be examined through objective physiological measurement of stress hormone levels and comparison of these levels between groups before and after the intervention.
- The intervention will be applied for one hour and only once during the first stage of labour after cervical dilatation of 6 centimetres.
- Blinding of the primigravidae mothers is not possible, and there may be bias in the self-assessed subjective outcomes such as the Visual Analog Scale.
- The expertise and experience of the nursing graduates who are trained to be the massage therapists is considered an important factor in the quality of treatment provided and this may underestimate the effect of BRM.

Word count 4,917 words

INTRODUCTION

Many primigravidae have reported experiencing various levels of pain during labour and high levels of anxiety about the labour process and its outcomes.[1–3] Anxiety escalating to fear is a common issue related to labour, especially among primigravidae.[4,5] Other recorded negative perceptions and psychological effects influencing labour experiences include distress and feelings of powerlessness during labour for women and their families.[5–7]

When poorly managed, labour pain may lead to severe consequences for women, such as prolonged labour,[5,8] which may increase the risk of foetal distress, head compression, intrauterine foetal death, low Apgar scores and physical injuries to neonates.[5,9] Prolonged labour results in increased risk of caesarean section, induced labour and assisted delivery using vacuum and forceps.[10,11] Studies have also reported negative mental impacts on women, sometimes even including postnatal post-traumatic stress disorder,[12,13] and subsequently reduced quality of life.[14] Feelings of anxiety often originate from possible birthing complications about which pregnant women have heard and read,[4,5,15,16] and may even result in women refusing normal vaginal delivery and insisting on caesarean sections without medical indications.[17] It is therefore important for healthcare professionals to assist and educate all expectant mothers on labour pain management.

Appropriate labour pain management and interventions are important aspects of obstetric care to ensure optimum outcomes for mothers and babies.[18] Pharmacologic interventions used in the management of labour pain include systemic sedatives, analgesics and regional anaesthesia.[19] Examples of these analgesics are aerosol and epidural opioids, intramuscular

pethidine (IMP) and intravenous sedatives.[20,21] Some of these are expensive and may be associated with adverse effects on mothers, the labour process and neonates.[22] In contrast, most non-pharmacological methods for labour pain management are simple and non-invasive, and are often cheaper and safer than pharmacological interventions.[23–25] Studies have found that non-pharmacological approaches, particularly breathing exercises, have positive impacts on relief of labour pain, [26–28] and anxiety in pregnant mothers.[29–31] This is especially true for Lamaze breathing, deep breathing exercises, [26–28,32,33] reflexology, [6,34] and massage.[35] Non-pharmacological approaches have been linked to shorter labour duration,[36] and improved new-born outcomes.[37] Our systematic review found that massage is beneficial for relieving labour pain,[38] and is associated with greater relaxation, higher alertness levels, improved mood and reduced stress hormone (cortisol) levels and anxiety symptoms.[39]

Rationale

It is hypothesised that the non-pharmacological approach of labour pain management occurs via the alteration of nociceptive stimuli and modification of the processing of nociceptive input at the central level, resulting in an overall improved sense of comfort and well-being, ultimately leading to stronger coping capabilities by the mothers in labour.[40]

The physiological mechanism of breathing is a protective action as it is a fight-or-flight reflex triggered by the central nervous system. Physiologically, deep abdominal breathing stimulates the parasympathetic nervous system. As a result, the blood circulation in pregnant women will undergo oxygenation, which will trigger the release of endorphins associated with decrease in heart rate and increase in feelings of calmness. At the same

time, endorphins can also suppress the sympathetic system, leading to a decrease in the release of stress hormones such as cortisol.[41, 42]

As for reflexology, so far there has been no constructive explanation of the underlying mechanism in reducing labour pain.[6,36] The reflexology therapist will apply pressure three times on specific points of the feet that are energetically connected to certain parts and organs of the body. As with skin-to-skin contact during massage, reflexology point pressure could trigger the release of endogenous endorphins and encephalins that help to reduce labour pain, stress, fatigue and anxiety.[43–46] Pressure on the solar plexus at the border of the upper and middle one-third of the sole is believed to facilitate the functions of the body's nervous system.[47] Pressure on the lower part of the forefoot reflects the heart and lungs. While pressure on the bridge of the foot reflects the liver and kidney and the heel will reflect the lower back, legs, pelvic region uterus, and intestines. The uterine point is believed to be located in the indented region between the inner ankles and the sole.[48] Therefore, it is believed to be helpful during labour. The pressure on toe and heel stimulate the reflex points in the pelvis. It is effective by releasing the oxytocin hormone which start and regulate the uterine contractions and relax during contractions.[49]

However, there are several postulated theories for its mechanism of action. Firstly, the autonomic-somatic integration theory suggests that the pressure applied to the feet during reflexology compresses the receptors in the cells, thus opening up the ionic channels in the plasma membrane and triggering a local action with the potential to convey messages to the spinal cord and/or brain.[46] The application of alternating pressure to the feet may also produce predictable reflexive actions within the nervous system and activate the

parasympathetic nervous system.[50] Based on the energy theory that moves toward the head from reflex points that stimulate the energy, neural paths, improve blood flow, release the endorphins and relief pain.[51] Another contemporary method explains that reflexology acts through "sympathetic resonance," in which an energy wave flows between therapist and client, promoting homeostatic balance.[52] This may occur through local enzymatic reactions on receptive fields or through an improved blood supply as a result of local skin temperature changes following the skin-to-skin contact.[47] Reflexologists also believe that the application of deep pressure on certain reflex points of the sole and palm may break any calcium crystals and uric acid accumulated in nerve endings that may cause blockages and induce pain.[53]

Reflexology also results in body relaxation and stimulation of any blocked nerve endings, which may propel any sluggish glands or organs to regain their normal functioning.[54] Ambiguity remains regarding the theories and mechanism of action of foot reflexology for labour pain, as compared to that for general pain.[6,35,36] Nonetheless, it is plausible to believe that reflexology techniques would have similar physiological effects for labour pain that bring about a sense of wellbeing, analgesia and subsequently the perception of pain relief.[37] Figure 1 summarizes the possible mechanisms of Reflexology therapy.

Massage therapy is another type of commonly used Complementary and Alternative Medicine (CAM) for the promotion of health and wellbeing.[35] Massage is a potent mechanical stimulus that produces a short-lived analgesic effect by activating the 'pain gate' mechanism.[55] Longer-lasting pain control appears to be mediated mainly by the descending pain suppression mechanism by activation of descending efferent pathways.[56]

The inhibition of pain-transmission neurons involves a combination of physiological and neurological mechanisms and it is commonly activated by noxious stimulation.[57] Figure 2 summarizes the possible mechanisms action of massage therapy.[58]

The three aforementioned therapies (i.e. BRM) for labour pain management have been shown to influence the secretion of certain stress hormones such as cortisol, adrenocorticotropic hormone (ACTH),[39,59] oxytocin (OT),[59] and possibly also the endorphins.[44,45] Endogenous oxytocin is a key component in the molecular pathways that buffer reaction to stress and decrease sensitivity to pain and inflammation,[60] cortisol is an important hormone released during stressful conditions.[39]

Significance of this clinical trial

Many studies have reported that not all pharmacologic and non-pharmacologic methods on their own are able to reduce labour pain satisfactorily. Despite the intervention, some mothers still endure some pain, anxiety and prolonged labour, and suffer from negative maternal and perinatal consequences.[5,15,16] From the perspective of complementary management, BRM are the techniques with the highest potential for managing pain and anxiety for primigravidae. Systematic reviews have concluded that CAM interventions to manage pain and anxiety during labour have often been biased and/or poorly executed, thus resulting in low quality of evidence,[61–64] or no strongly supported evidence.[65–67] Therefore, there is a need for a rigorous and robust trial to examine the effect of the combined intervention of BRM on labour pain, anxiety, stress hormones, V/S, FHR, duration of

labour, Apgar Scores and maternal satisfaction among the primigravidae using multiple relevant outcome measures.

METHODS AND DESIGN

This study aims to investigate the combined effect of BRM on labour pain, duration of labour, anxiety, maternal satisfaction, stress hormones, and new-born outcome among primigravidae in Saudi Arabia. The specific objectives are 1) to compare the effect of the combined breathing exercise, foot reflexology, and back massage (intervention) on labour pain intensity, anxiety level, duration of labour, maternal satisfaction, stress hormones, and neonatal outcome compared to the standard midwifery care (control); 2) to identify the predictors of pain, anxiety, duration of labour, the satisfaction of mother, and neonatal outcome from the baseline sociodemographic and obstetric characteristics.

Study Design

The study design will be a single-blind parallel randomised controlled trial (RCT), in which participants are randomly assigned to receive either the BRM intervention or control care.

Study Setting

This study will be conducted in the Makkah Maternity and Children Hospital (MCH) in Makkah, Saudi Arabia. The hospital is a tertiary-level, governmental referral hospital with special services for paediatrics, gynaecology, and obstetrics.[68] In Saudi Arabia, almost all tertiary hospitals, including our study site, offer systemic pharmacologic agents, either intravenous or intramuscular analgesics to manage pain during labour;[69] however, providing non-invasive and non-pharmacological methods of pain relief during labour are

not common practices.[69] To our best knowledge, the combined effect of BRM on primigravidae has not been investigated at any Saudi Arabia hospital prior to this trial.

Participants

The study participants will include primigravidae, age 20–35 years old, at 37 to 41 weeks of gestation, and in the first stage of labour. The inclusion criteria include singleton pregnancy, cephalic presentation, and regular contraction. In labour, the participants must achieve six centimetres of cervical dilatation, with a minimum of three contractions of at least moderate intensity every 10 minutes, in which the duration of the contraction must be between 30–60 seconds.

The exclusion criteria include diagnosis of underlying chronic diseases such as cardiovascular disease, kidney disease, diabetes, asthma, mental health disorders, epilepsy or seizure; pregnancy-related diseases such as gestational diabetes, preeclampsia, cephalo-pelvic disproportion, polyhydramnios or oligohydramnios or deep venous thrombosis; and pregnancy complications such as placenta praevia, antepartum haemorrhage, fetal distress or being put on analgesics other than IMP.

Recruitment

Recruitment will be conducted at the antenatal clinic at the trial site. Only those who plan to deliver in the trial hospital's delivery room will be further briefed and assessed for their eligibility. At this hospital, antenatal mothers are given monthly follow-up appointments

until 28 weeks' gestation. The frequency increases to bi-weekly until 32 weeks' gestation; then patients are seen weekly until delivery.

For this study, we will approach primigravidae between 26 to 34 weeks of gestation in equal numbers based on the gestational weeks. This means that about an equal number of primigravidae at week of gestation of 26, 28, 30, 32 and 34 will be recruited in order to spread out the occurrence of labour in the subsequent 2–3 months to increase the feasibility of the BRM intervention. Because participant recruitment and the training of the research team members is estimated to last up to two to three months, women of 34+ weeks gestation cannot be recruited during this period because they will inevitably go into labour before the research preparations are complete.

At the antenatal clinic, the principal investigator will provide general health education about pain management during labour. The participant information sheet of this RCT will be provided for the eligible patients. If they are interested in participating, they will sign a written consent form and will be identified by a unique stamp on their antenatal cards. When the participants arrive in the labour room for delivery, they will be re-evaluated for the eligibility.

Randomisation

Since IMP is a commonly prescribed analgesic in labour and may have substantial effects on the primigravidae and neonates, randomisation will be stratified according to the administrative status of IMP. This will ensure the same numbers of primigravidae with and

without IMP in the intervention and control groups. To achieve this, we use a block of size 4 with a 1:1 allocation ratio, leading to a possibility of 6 permutations. All possible block sequences will be randomly generated with the help of free software from the internet https://www.sealedenvelope.com/simple-randomiser/v1/. A random list will be created after the sample size number, treatment groups, block sizes, list length, and stratification factors are entered into the software. The order of the subjects will be used by the research coordinator who will be stationed in the delivery room to conduct the random group allocation for primigravidae in labour who have achieved a cervical dilation of 6 cm. The principal investigator, outcome assessors, and massage therapist in this trial will not be involved in the allocation of the interventional groups. Figure 3 outlines the CONSORT flow diagram.

Data Collection

Every questionnaire will be coded with a unique number. Data collection in the delivery room will be facilitated by the trained research coordinator and two outcome assessors. The outcome assessors will be assigned to the control or the intervention group on the same day. Once the form is completed by the outcome assessors, it will be kept by the research coordinator in a safe location in the delivery room.

Throughout all of the outcome assessment time points, a massage therapist will be present in the delivery room of both the intervention and control groups. For the intervention group, the primigravidae in labour will receive the BRM intervention from the massage therapist. For the control group, the practicing midwife will perform routine labour care such as touch therapy, ensuring that the mother lies on her left side, and providing encouragement and

counselling. The outcome assessor will measure and assess both the intervention and control groups at the same time points. Both groups will be equipped with similar extra equipment. This blinding effort is intended to minimize biases during the outcome assessment. However, blinding of the participants will be impossible due to the nature of the intervention.

Interventions

The BRM intervention consists of 5 minutes of breathing exercise followed by 10 minutes of foot reflexology on each sole and 35 minutes of continuous massage over the lower limbs and back. The massage therapist will allow the primigravidae to lie on the left side,[70] to move and change her position during the intervention and answer any question or inquiry. Table 1 provides a detailed explanation of the BRM intervention procedure. As for the control group, the primigravidae in labour will receive routine labour room care.

Training for the research team members

A total of 13 research assistants will be recruited and trained for the intervention and data collection from June to December 2019, (Figure 4). They will be given the BRM training for one week by the principal investigator who has completed the professional massage and reflexology training at a certified training centre in Malaysia (Tim Body Care Training Centre 1403695-D) for six months including training and working.

Study Outcomes and Measures

There are eight outcomes: two primary outcomes and six secondary outcomes. The two primary outcomes are pain intensity and anxiety level (See Table 2). Pain intensity is measured with the Present Behavioural Intensity (PBI)[71,72] and the self-report Visual Analog Scale (VAS),[73–77] while anxiety is measure with Anxiety Assessment Scale for Pregnant Women in Labour (AASPWL).[78]

The outcome assessor will ask the pregnant women to pick a colour on an A-4 sized paper that contains six different coloured parts, from no pain (score 1) to most severe pain (score 6) based on her level of pain.[76,79] The researcher selected the VAS questionnaire because it is an acceptable tool and relatively easy to administer to women in labour. Pain intensity will be measured at baseline before the intervention, and multiple times during and after contractions (Figure 5a). During the intervention, pain intensity will be measured after the breathing exercise and foot reflexology therapy (after 25 minutes from the start of the intervention), followed by another assessment halfway through the massage therapy (after 45 minutes) during and after contraction. Pain intensity will be measured for every participating primigravidae in both the intervention and control group. For the control group, pain intensity will be measured first at baseline before the intervention at 6 cm. During the intervention, pain intensity will be measured after 25 minutes from the start of the intervention time, followed by another assessment after 45 minutes, during and after contraction. Upon completion of the intervention, the measurement will be taken immediately, and twice hourly thereafter during the first stage of labour (Figure 5b).

The AASPWL will be used to assess anxiety during labour. The anxiety level will be measured at cervical dilatation of 6cm, after the completion of the interventions, and twice every 60 minutes during the first stage of labour. For the control group, the assessment will be performed when the cervix is at 6 cm, after one hour (synchronized to the completion of the intervention in the intervention group), and twice every 60 minutes during the first stage of labour (Figure 5b).

The secondary outcomes measured in the RCT include maternal stress hormones level, maternal V/S, FHR, duration of labour, neonatal Apgar score, and maternal satisfaction[80] (See Table 3).

The stress hormones level will be measured at baseline, and again one and a half hour after the patient has reached 6 cm of cervical dilatation (Figure 5). Blood samples will again be taken by midwives on duty in the delivery room. This will occur after the BRM intervention in the intervention group (Figure 5a), and at the same time in the control group (Figure 5b). The research assessors will collect an 8 ml blood sample in a plain tube, of which 3mls is for ACTH, 3mls for cortisol, and 2mls for OT hormones; it will be sent immediately to the MCH laboratory to carefully avoid any haemolysis of the samples. Hormones will be analysed by the sandwich ELISA technique using commercial kits by Cobas e411 Analyzer (HITACHI, USA) for ACTH hormone, and Abbot Architect I200 Analyzer (Abbott, USA) for Cortisol and OT hormones.

Since cortisol levels follow a diurnal variation or circadian rhythm where the hormone levels peak in the morning and fall at night, and vary in accordance with a number of factors

including age, time of day, stress level, sample type, laboratory location and the method used for testing,[81,82] we will use a chart from the laboratory to verify the normal cortisol range in the morning, noon, afternoon, evening, or night, and compare these ranges to the blood samples taken to determine whether the blood test results of the participants before and after the intervention are high, normal or low.

ACTH and cortisol levels are interrelated. When the cortisol levels are at their peak, ACTH levels generally fall and vice versa.[83] Hence, it may be understood that ACTH and cortisol have corresponding levels at any given point of time. This provides a relative value for both stress hormones. With regard to OT, the blood sample test for the pregnant woman will be higher if she receives an infusion of OT during intervention.[84,85] If the events are equal in both groups, we will proceed to the analysis as planned. If the events are many and unequal in both groups, we will either conduct a separate statistical analysis stratified according to the event of OT infusion. If the number of event occurrences is low, we may exclude these participants and analyse the outcome as planned. However, the author will investigate the oxytocin level before and after applying the BRM in addition to childbirth. Oxytocin increases with contraction and hypothetically with and after BRM. The oxytocin will increase in the second stage, inhibit the Stress hormones, and will increase after apply the BRM.

Maternal V/S and FHR will be collected twice at 6cm cervical dilatation and immediately post-BRM for the intervention group, and the same data will be collected at the same timing for the control groups. The Apgar Scores (taken from the delivery room medical record)

and maternal satisfaction will be measured only once at the completion of the childbirth, before the transfer of the mother from the delivery room to the postnatal ward.

Sample size

The sample size estimation was based on a review of similar literature on pain and anxiety as outcomes, and calculated using G*power free software.[86] We estimated an effect size of 0.6 on anxiety mean score reduction in the intervention group compared to the control,[86] as this gives a larger required sample size compared to that based on the primary outcome of pain. Thus, with the power of 95% at α error 0.05, the required sample size is 128 for the two groups. It is further inflated to 154 to account for a predicted 20% attrition rate. Therefore, a minimum number of 77 primigravidae will be recruited for each group.

Statistical analysis

Data will be entered by a blinded enumerator. The database will be checked for accuracy before analysis. The principal investigator has the overall responsibility for the compilation, maintenance, and management of the study database. The analysis will be performed using IBM Statistical Package for Social Science (SPSS) version 25.

Descriptive statistical analysis will be performed according to the distribution of the data, using means and standard deviations for data with normal distribution, and median and inter-quartile ranges for data that are not normally distributed. Normality testing will be conducted for all continuous variables using different methods such as Histogram and p-p plot. Categorical variables will be reported in frequencies and percentages.

The differences between the groups and times level will be analysed using a Generalised Linear Mixed Model (GLMM). GLMM is appropriate where repeated measurements are made on the same statistical units. GLMM will also be used to accommodate non-normal distribution in outcome data. The variables of time in a categorical form, intervention group, group*time interaction, and the baseline random part of the model will include a random intercept and an unstructured correlation matrix for the correlation of measurements within pregnant women. The fixed part of the model will include pain score, whereby the difference in pain score at every time point will be tested using a linear contrast. We will take the pain intensity measured with PBI and VAS at one-hour post intervention as the main co-primary outcomes. This is because the effects of the massage and reflexology will still be observable, and thus the intervention group can be fairly compared to the control group.[46,50–53]

Any significant baseline imbalances will be adjusted for in the analysis. If necessary, multiple imputations will be conducted for the missing data. A calculated 95% confidence interval and two-sided α of 0.05 will be used to test significance. In addition, we will analyse PBI and VAS at the same time points and measure the agreement between PBI and VAS by using the Spearman correlation coefficient and interclass correlation. We will analyse other outcomes using the same statistical strategy mentioned above. Additionally, we will conduct time series analyses to examine the patterns of change in the outcomes between the two groups and after BRM intervention.

The independent effect(s) of socio-demographic and obstetric characteristics on each primary and secondary outcome at one-hour post-intervention will be analysed using multiple linear regression analyses.

DISCUSSION

Safe and efficient pain management is important for pregnant women and their families,[18] and different types of CAM have been shown to be beneficial to reduce or alleviate labour pain. However, evidence is scarce regarding the effects of combined therapies.[87] Therefore, we designed this trial to study the effects of BRM on labour pain and other psychological and physiological impacts among primigravidae. The study protocol for the RCT is to determine the combined effect of BRM on the intensity of pain and level of anxiety in primigravidae during the first stage of labour. Additional outcomes that will be assessed include stress hormones, maternal VS, FHR, duration labour, neonatal Apgar score, and maternal satisfaction.

In this study, the intervention will be applied only once and only during the first stage of labour even though the first stage of labour among primigravidae takes approximately 8–12 hours. By timing the intervention after cervical dilation of 6 cm, the effect of the combined BRM could exert its greatest influences (if any) on the labour experience of the primigravidae and neonatal outcome, because this period is believed to accompany the highest levels of labour pain.[88,89]

We will assess the outcomes using a mixture of subjective and objective tools. For example, pain intensity and anxiety levels are subjective measurements, based on the personal feelings and judgments of the respondents. Duration of labour, neonatal Apgar score, and maternal stress hormones level of ACTH, cortisol, and oxytocin are objective measurements that will indicate the stress response to the BRM intervention conducted on the primigravidae. This is one of the strengths of our study.

VAS is one of several ways of measuring the effectiveness of BRM, and is a commonly used graphic rating method.[70,78] However, VAS might not be the gold standard to measure labour pain, given the inconsistency of its results and its ceiling effect.[78,90] Recognizing this inadequacy, we will ensure that the participants understand the VAS scoring at admission to the delivery room before they are asked to indicate their pain level later. Labour pain outcome will also be measured via pain intensity assessment using the PBI,[74] which will be rated by outcome assessors. Multiple measurements will be taken during and after contraction, and before and after the intervention. There will also be other outcomes, related to maternal response to pain, namely anxiety level and maternal stress hormones.[91]

This study has several other limitations. First, the intervention will be performed for one hour, during which it may be interrupted by routine medical care such as regular vaginal examinations, V/S measurements, and FHR monitoring. However, we believe that this will not reduce the effect of the BRM intervention, because we can start the BRM before or after the labour care routine. Second, the process of labour and birthing is unpredictable even if the participants are low-risk. In certain instances, the process of the intervention might not go well as planned and this may reduce the sample size. Some patients may end

up needing a caesarean section, and some may suffer from other obstetric complications during delivery. As a result, we have inflated the sample size accordingly. Third, the results from this study will not be generalisable to multigravidae as we include only primigravidae. Nevertheless, we believe that primigravidae will benefit the most from the intervention as they are likely to experience a higher level of labour pain and a longer duration of labour compared to multigravidae. Fourth, placebo effects can influence patient outcomes after (CAM), resulting in high rates of good outcomes, which may be wrongly attributed to specific treatment effects.[92]

We recognise that the expertise and experience level of the reflexologist is an important factor in the quality of treatment provided and this may affect the outcomes of the BRM. The massage therapists and the outcome assessors will be given the appropriate training on the BRM for one week by the principal investigator who attended a professional training and was certified. After the training, they will be tested in a pilot study to ensure their competency in performing the BRM. Additional quality control measures for the outcome assessors are planned, as they will be assigned to the control delivery room or the intervention delivery room on the same day. All of the completed assessment forms will be reviewed and kept by the research coordinator in a safe location in the delivery room. Any issues on the form such as blank spaces and extreme values will be immediately clarified and resolved.

In addition to labour pain, this study will assess the anxiety level of pregnant mothers. Unlike labour pain, anxiety level can be affected by individual characteristics, previous life

experiences, and other environmental causes.[93] However, we believe that these factors will not play a significant role after effective randomisation.

Apart from the actual labour experience, there are a few other external factors that may affect maternal satisfaction, such as the delivery room services, the health of the baby, the gender of the child, family support, and other psychosocial factors. As satisfaction is a multi-dimensional and complex feeling, it is difficult to measure with a single tool and to narrow it down to only the first stage of labour.

It is understood that a birthing process is a natural event, especially for low-risk women. Thus, the management of labour should be conducted in a supportive manner with minimal or no interferences. This study will provide high-quality evidence about the effects of the combined BRM for labour pain management. These findings will be important for hospitals offerings for expectant mothers in providing a rationale for their decisions about which alternative treatments to offer, to primigravidae and their family members during decision making about labour pain management.

Acknowledgements

The authors would like to acknowledge the assistance provided by Um-Al-Qura University, the Research Department in the Directorate of Health Affairs, Makkah Region, and Saudi Arabia Culture Mission in Saudi Arabia. Also, we would like to acknowledge Enago for the English language editing services for this report.

Author Contributions

KB drafted, formulated, and submitted the manuscript. All authors MHR, AHI, LK & BHC contributed to the study designs, read, revised, and approved the research protocol critically for important intellectual content and helped to draft the final manuscript. All authors approved the final manuscript for submission. Authorship eligibility is in accordance with the International Committee of Medical Journal Editors (ICMJE) guidelines.

Funding

This work was supported by the Umm Al-Qura University and Saudi Arabia Culture Mission (SACM). The author (KB) is a student who owns a Financial Guarantee, which covers the study and research process. The Financial Guarantee will cover all the research's payments. The funders will not be involved in the study design, data collection, analysis and interpretation of the data and writing of the manuscript.

Competing Interest

None declared.

Patient Consent for Publication

Not applicable since this is a study protocol.

Availability of Data and Materials

The datasets will be available from the corresponding author on reasonable request. The data will be kept for a maximum period of two years from the end of data analysis and will be placed in a sealed envelope that will remain with the primary author. Subsequently, the

forms will be destroyed via a shredding machine located at UPM in the presence of my supervisor and some academic staff. The soft copy and record data, as well as the questionnaires and database of hard copy will be deleted, and we will re-setup windows in the computer to destroy the database after a maximum period of two years.

Ethics Approval and Consent to Participate

Ethics approval was obtained from the Ethical Committee for Research Involving Human Subjects of the Ministry of Health in the Saudi Arabia (H-02-K-076-0319-109) on 14 April 2019, and from the Ethics Committee for Research Involving Human Subjects (JKEUPM) Universiti Putra Malaysia on 23 October 2019, reference number (JKEUPM-2019-169). Additional administrative approval will be requested from the medical director of the Makkah Maternity and Children Hospital. The participant information sheet for the pregnant women will be also provided. If they are interested and eligible to participate, pregnant women will sign consent forms. Consent form contains purpose of this study, procedures involved in the research pre and post intervention. They will inform the potential benefits and risk of the intervention research. Participants will be given an affirmation of confidentiality and protection the data collection. The results won't be disseminated to the study participants, except If one of the participants would like to know her results, her mobile number will be taken and a message will be sent.

Patient and Public Involvement

Patients are involved in the questionnaire's face and content validity testing. Based on feedback from the patients in a pilot study, improvement to the questionnaires' approaches and trial processes will be implemented. Patient preferences were not directly obtained

with regard to choosing the BRM intervention; this was based on the principal investigator's practice experience and encounters with pregnant women. However, the patients will be involved in the recruitment to and conduct of the study. They will attend antenatal class and agreement by consent to share in this study. Also, they will answer all questionnaires pre and post the intervention. In addition, they will need to agree to BRM as the intervention.

Reference

1. Gibson E. Women's expectations and experiences with labour pain in medical and midwifery models of birth in the United States. *Women and Birth* 2014;**27**:185–9. https://doi.org/10.1016/j.wombi.2014.05.002.

2. Beigi NMA, Broumandfar K, Bahadoran P, et al. Women's experience of pain during childbirth. *Iran J Nurs Midwifery Res* 2010;**15**:77–82.

3. Devilata T, Swarna S. Effectiveness of pre delivery preparation on anxiety among Primigravida mothers at maternal child health centre Tirupati, AP, India. *IOSR J Nurs Heal Sci* 2015;**4**:19-24. https://doi.10.9790/1959-04651924.

4. Aksoy M, Aksoy AN, Dostbil A, et al. The Relationship between Fear of Childbirth and Women ' s Knowledge about Painless Childbirth. *Obstet Gynecol Int* 2014;**2014**:7. http://dx.doi.org/10.1155/2014/274303

5. Nystedt A, Hildingsson I. Diverse definitions of prolonged labour and its consequences with sometimes subsequent inappropriate treatment. *BMC Pregnancy Childbirth* 2014;**14**:233. https://doi.org/10.1186/1471-2393-14-233

6. Hanjani SM, Tourzani ZM, Shoghi M. The Effect of Foot Reflexology on Anxiety , Pain , and Outcomes of the Labor in Primigravida Women. *Acta Med Iran* 2014;**53**:507–511.

7. Li W, Zhang H, Ling Y, et al. Effect of prolonged second stage of labor on maternal and neonatal outcomes. *Asian Pac J Trop Med* 2011;**4**:409–411. https://doi.org/10.1016/S1995-7645(11)60114-4

8. Neal JL, Lamp JM, Buck JS, et al. Outcomes of Nulliparous Women with Spontaneous Labor Onset Admitted to Hospitals in Pre-active versus Active Labor. *J Midwifery Womens Heal* 2014;**59**:28–34. doi:10.1111/jmwh.12160.Outcomes

9. Kjærgaard H, Olsen JØRN, Ottesen B, et al. Incidence and outcomes of dystocia in the active phase of labor in term nulliparous women with spontaneous labor onset. *Acta Obstet Gynecol* 2009;**88**:402-407. doi:10.1080/00016340902811001

10. Lowe NK. A Review of Factors Associated With Dystocia and Cesarean Section in Nulliparous Women. *J Midwifery Women's Heal* 2007;**52**:216–228. doi:10.1016/j.jmwh.2007.03.003

11. Shields SG, Ratcliffe SD, Fontaine P, et al. Dystocia in nulliparous women. *Am Fam Physician* 2007;**75**:1671–1678.

12. Garthus-Niegel S, Knoph C, von Soest T, et al. The Role of Labor Pain and Overall Birth Experience in the Development of Posttraumatic Stress Symptoms: A Longitudinal Cohort Study. *Birth* 2014;41:108–115. https://doi.org/10.1111/birt.12093

13. Peeler S, Stedmon J, Chung MC, et al. Women's experiences of living with postnatal PTSD. *Midwifery* 2018;**56**:70–78. https://doi.org/10.1016/j.midw.2017.09.019

14. Boryri T, Noori NM, Teimouri A, et al. The perception of primiparous mothers of comfortable resources in labor pain (a qualitative study). *Iran J Nurs Midwifery Res* 2016;**21**:239–246. https:// doi.org/10.4103/1735-9066.180386

15. Størksen HT, Garthus-niegel S, Adams SS, et al. Fear of childbirth and elective caesarean section : a population-based study. *BMC Pregnancy Childbirth* 2015;**15**:221. https://doi.org/10.1186/s12884-015-0655-4

16. Stoll KH, Hauck YL, Downe S, et al. Preference for cesarean section in young nulligravid women in eight OECD countries and implications for reproductive health education. *Reprod Health* 2017;**14**:116. https://doi.org/10.1186/s12978-017-0354-x

17. El-Aziz SNA, Mansour SE, Hassan NF. Factors associated with fear of childbirth: It's effect on women's preference for elective cesarean section. *J Nurs Educ Pract* 2017;**7**:133–45. https://doi.org/10.5430/jnep.v7n1p133.

18. Lowe NK. The Pain and Discomfort of Labor and Birth. *J Obstet Gynecol Neonatal Nurs* 1996;**25**:82–92. https://doi.org/10.1111/j.1552-6909.1996.tb02517.x

19. Rayburn WF, Zuspan FP. *Drug therapy in obstetrics and gynecology*. 3rd ed. St. Louis: : Mosby 1992.

20. Ullman R, Smith LA, Burns E, et al. Parenteral opioids for maternal pain management in labour. Cochrane Database *Syst Rev* 2010;9. https://doi.org/10.1002/14651858.CD007396.pub2

21. Pereira RR, Kanhai H, Rosendaal F, et al. Parenteral Pethidine for labour pain relief and substance use disorder : 20-year follow-up cohort study in offspring. *BMJ Open* 2012;**2**:e000719. http://dx.doi.org/10.1136/bmjopen-2011-000719

22. Smith LA, Burns E, Cuthbert A. Parenteral opioids for maternal pain management in labour. Cochrane Database *Syst Rev* 2018;6. https://doi.org/10.1002/14651858.CD007396.pub3

23. Simkin P. Reducing Pain and Enhancing Progress in labor : A Guide to Nonpharmacologic Methods for Maternity Caregivers. *Birth* 1995;**22**:161–71. https://doi.org/10.1111/j.1523-536X.1995.tb00693.x

24. Cook A, Wilcox G. Pressuring Pain: Alternative Therap for Labor Pain Management. AWHONN *Lifelines* 1997;**1**:36–41. https://doi.org/10.1111/j.1552-6356.1997.tb00929.x

25. Jones LV. Non-pharmacological approaches for pain relief during labour can improve maternal satisfaction with childbirth and reduce obstetric interventions. *Evid Based Nurs* 2015;**18**:70. http://dx.doi.org/10.1136/eb-2014-101938

26. Busch V, Magerl W, Kern U, et al. The Effect of Deep and Slow Breathing on Pain Perception , Autonomic Activity , and Mood Processing -An Experimental Study. *Pain Med* 2012;**13**:215–28. https://doi.org/10.1111/j.1526-4637.2011.01243.x

27. Thomas ME, Dhiwar MS. Effectiveness of Patterned Breathing Technique in Reduction of Pain During First Stage of Labour Among Primigravidas. Sinhgad E-*Journal Nurs* 2011;**1**:6–8.

28. Kaur K, Rana AK, Gainder S. Effect of video on ' Breathing Exercises during labour ' on Pain Perception and Duration of Labour Among Primigravida Mothers. *Nurs Midwifery Res Journa* 2013;**9**:1–9.

29. El-refaye GE, El Nahas EM, Ghareeb HO. Effect of kinesio taping therapy combined with breathing exercises on childbirth duration and labor pain : a randomized controlled trial. *Bull Fac Phys Ther* 2016;**21**:23–31. https:// doi.10.4103/1110-6611.188026

30. Chuang LL, Lin LC, Cheng P, et al. Effects of a relaxation training programme on immediate and prolonged stress responses in women with preterm labour. *J Adv Nurs* 2011;**68**:170–80. https://doi.org/10.1111/j.1365-2648.2011.05765.x

31. Akbarzadeh M, Sharif F, Zare N. The Reduction of Anxiety and Improved Maternal Attachment to Fetuses and Neonates by Relaxation Training in Primigravida Women. *Women's Heal Bull* 2014;**1**:e18968. https://doi.org/10.17795/whb-18968.

32. Nattah FM, Abbas WAK. Assessment of Level of Pain and its Relation with Breathing Exercise in the First Stage of Labour among Primi Mothers at Hilla Teaching Hospital. *Eur J Sci Res* 2016;**135**:121–8.

33. Yuksel H, Cayir Y, Kosan Z, et al. Effectiveness of breathing exercises during the second stage of labor on labor pain and duration : a randomized controlled trial. *J Integr Med* 2017;**15**:456–61. https://doi.org/10.1016/S2095-4964(17)60368-6

34. Mathew AM, Francis F. Effectiveness of Foot Reflexology in Reduction of Labour Pain among Mothers in Labour Admitted at PSG Hospital, Coimbatore. *Int J Nurs Educ* 2016;**8**:11–5. https://doi.org/10.5958/0974-9357.2016.00081.7

35. Cohen M. The effectiveness of massage therapy a summary of evidence-based research. Melbourne:australian associaiton of massage therapy. Melbourne: : Australian Association of Massage Therapists 2011.

36. Dolatian M, Hasanpour A, Montazeri S, et al. The effect of reflexology on pain intensity and duration of labor on primiparas. *Iran Red Crescent Med J* 2011;**13**:475–479.

37. Valiani M, Shiran E, Kianpour M, et al. Reviewing the effect of reflexology on the pain and certain features and outcomes of the labor on the primiparous women. *Iran J Nurs Midwifery Res* 2010;**15**:302–310.

38. Baljon K, Romli MH, Ismail AH, et al. The Effectiveness of complementary and alternative medicine of massage and reflexology in managing pain and anxiety among primigravidas in labor: a systematic review. [in preparation for submission to a journal]

39. Field T, Hernandez-Rief M, Diego M, et al. Cortisol decreases and serotonin increases following massage therapy. *J Neurosci* 2005;**115**:1397–413. https://doi.org/10.1080/00207450590956459

40. Crowe K, von Baeyer C. Predictors of a Positive Childbirth Experience. *Birth Iss Perinat C* 1989;**16**:59–63. https://doi.org/10.1111/j.1523-536X.1989.tb00862.x

41. Ma X, Yue ZQ, Gong ZQ, et al. The effect of diaphragmatic breathing on attention, negative affect and stress in healthy adults. *Front Psychol* 2017;**8**:1–12. https://doi.org/10.3389/fpsyg.2017.00874

42. Bordoni B, Purgol S, Bizzarri A, et al. The Influence of Breathing on the Central Nervous System. *Cureus* 2018;**10**:1–8. https://doi.org/10.7759/cureus.2724

43. ElFattah AH, Metwaly S, Khedr N. Outcomes of foot reflexology on the pain and certain features of the labor for the primiparous women. *Life Sci J* 2015;**12**:206–16.

44. Vigotsky AD, Bruhns RP. The role of descending modulation in manual therapy and its analgesic implications: a narrative review. *Pain Res Treat* 2015;**2015**:292805. https://doi.org/10.1155/2015/292805

45. Kaada B, Torsteinbø O. Increase of plasma beta-endorphins in connective tissue massage. *Gen Pharmacol* 1989;**20**:487–489. https://doi.org/10.1016/0306-3623(89)90200-0

46. Tiran D, Chummun H. The physiological basis of reflexology and its use as a potential diagnostic tool. *Complement Ther Clin Pract* 2005;**11**:58–64. https://doi.org/10.1016/j.ctnm.2004.07.007

47. Embong NH, Soh YC, Ming LC, et al. Revisiting reflexology: Concept, evidence, current practice, and practitioner training. *J Tradit Complement Altern Med* 2015;**5**:197–206.

48. Levy I, Attias S, Lavee TS, et al. The effectiveness of foot reflexology in reducing anxiety and duration of labor in primiparas: An open-label randomized controlled trial. *Complement Ther Clin Pract* 2020;**38**:101085. https://doi.org/10.1016/j.ctcp.2019.101085

49. Yılar Erkek Z, Aktas S. The effect of foot reflexology on the anxiety levels of women in labor. *J Altern Complement Med Medicine*, 2018;**24**:352–60. https://doi.org/10.1089/acm.2017.0263

50. Tappan FM, Benjamin PJ. *Tappan's handbook for healing massage techniques. Classic, Holistic, and Emerging Methods*. 3rd Ed. Stamford, US : : Appleton & Lange

1998.

51. Taheri H, Naseri-Salahshour V, Abedi A, et al. Comparing the effect of foot and hand reflexology on pain severity after appendectomy: A randomized clinical trial. *Iran J Nurs Midwifery Res* 2019;**24**:451–456. ttps://doi.org/10.4103/ijnmr.IJNMR_85_18

52. Tiran D, Evans M. Theoretical background to structural reflex zone therapy. In: Tiran D, ed. *Reflexology in Pregnancy and Childbirth*. London: : Elsevier 2010. 1–22.

53. Poole H, Glenn S, Murphy P. A randomised controlled study of reflexology for the management of chronic low back pain. *Eur J Pain* 2007;**11**:878–87. https://doi.org/10.1016/j.ejpain.2007.01.006

54. Keet L. *The reflexology bible*. 1st ed. London: : Octopus publishing group 2008.

55. Roudaut Y, Lonigro A, Coste B, et al. Touch sense: functional organization and molecular determinants of mechanosensitive receptors. *Channels* 2012;**6**:234–45. https://doi.org/10.4161/chan.22213

56. Goats GC. Massage--the scientific basis of an ancient art: Part 2. Physiological and therapeutic effects. *Br J Sports Med* 1994;**28**:153–6. http://dx.doi.org/10.1136/bjsm.28.3.153

57. Basbaum AI, Fields HL. Endogenous pain control mechanisms: Review and hypothesis. *Ann Neurol* 1978;**4**:451–62. http://dx.doi.org/10.1002/ana.410040511

58. Weerapong P, Hume PA, Kolt GS. The mechanisms of massage and effects on performance, muscle recovery and injury prevention. *Sport Med* 2005;**35**:235–56. http://dx.doi.org/10.2165/00007256-200535030-00004

59. Morhenn V, Beavin LE, Zak PJ. Massage Increases Oxytocin and Reduces Adrenocorticotropin Hormone in Humans. *Altern Ther* 2012;**18**:11–8.

60. Li Q, Becker B, Wernicke J, et al. Foot massage evokes oxytocin release and activation of orbitofrontal cortex and superior temporal sulcus. *Psychoneuroendocrinology* 2018;**101**:193–203. http://dx.doi.org/10.1016/j.psyneuen.2018.11.016

61. Bell AF, Erickson EN, Carter CS. Beyond Labor: The Role of Natural and Synthetic Oxytocin in The Transition To Motherhood. *J Midwifery Womens Hea*l 2015;**59**:35–42. http://dx.doi.org/10.1111/jmwh.12101

62. Hu J, Brettle A, Jiang Z, et al. A systematic review and meta-analysis of the effect of massage therapy in pain relief during labor. *J Nurs* 2017;**6**:1–14. http://dx.doi.org/10.18686/jn.v6i4.130

63. Huntley AL, Coon JT, Ernst E. Complementary and alternative medicine for labor pain : A systematic review. *Am J Obstet Gynecol* 2004;**191**:36–44. http://dx.doi.org 10.1016/j.ajog.2003.12.008

64. Ranjbaran M, Khorsandi M, Matourypour P, et al. Effect of Massage Therapy on Labor Pain Reduction in Primiparous Women A Systematic Review and Meta-analysis of Randomized Controlled Clinical Trials in Iran. *Iran J Nurs Midwifery Res* 2017;**22**:257–61.

65. Smith CA, Levett KM, Collins CT, et al. Massage , reflexology and other manual methods for pain management in labour. *Cochrane Database Rev* 2018. https://doi.org/10.1002/14651858.CD009290.pub3

66. Kirkham M. *The Midwife-Mother Relationship*. 2nd ed. Hampshire: : Red Globe Press 2000.

67. Levett KM, Smith CA, Bensoussan A, et al. The Complementary Therapies for Labour and Birth Study: Making sense of labour and birth – experiences of women, partners and midwives of a complementary medicine antenatal education course. *Midwifery* 2016;**40**:124–131. http://dx.doi.org/10.1016/j.midw.2016.06.011

68. Ministry of Health Saudi Arabia. Maternity and Children Hospital Makkah. 2013. http://www.testonserver.com/mch/ (accessed November 27, 2018).

69. Altaweli RF, McCourt C, Baron M. Childbirth care practices in public sector facilities in Jeddah, Saudi Arabia: A descriptive study. *Midwifey* 2014;**30**:899–909. http://dx.doi.org/10.1016/j.midw.2014.03.006

70. Farine D, Seaward PG. When it comes to pregnant women sleeping, is left right? *J Obstet Gynaecol Can* 2007;**29**:841–842.

71. Bonnel AM, Boureau F. Labor Pain Assessment : Validity of a Behavioral Index. *Pain* 1985;**22**:81–90. https://doi.org/10.1016/0304-3959(85)90150-2

72. Chang M, Wang S, Chen C. Effects of massage on pain and anxiety during labour : a randomized controlled trial in Taiwan. *J Adv Nurs* 2002;**38**:68–73.

73. Mårtensson L, Bergh I. Effect of treatment for labor pain : Verbal reports versus visual analogue scale scores - A prospective randomized study. *Int J Nurs Midwifery* 2011;**3**:43–7.

74. Bahammam MA, Hassan MH. Validity and reliability of an Arabic version of the modified dental anxiety scale in Saudi adults. *Saudi Med J* 2014;**35**:1384. http://dx.doi.org/10.2466/pr0.1997.80.3.947

75. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: Visual analog scale for pain (vas pain), numeric rating scale for pain (nrs pain), mcgill pain questionnaire (mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap). *Arthritis Care Res* 2011;**63**:S240–S252. doi:10.1002/acr.20543

76. Taghinejad H, Delpisheh A, Suhrabi Z. Comparison between massage and music therapies to relieve the severity of labor pain. *Womens Health* 2010;**6**:377–381. https://doi.org/10.2217/WHE.10.15

77. Jensen MP, Karoly P, Braver S. The Measurement of Clinical Pain Intensity : a Comparison of Six Methods. *Pain Res Manag* 1986;**27**:117–26. https://doi.org/10.1016/0304-3959(86)90228-9

78. Durat G, Çulhacik GD, Doğu Ö, et al. The development of an anxiety assessment scale for pregnant women in labor. *Saudi Med J* 2018;**39**:609–14. http://dx.doi.org/10.15537/smj.2018.6.22266

79. Wei CK, Leng CY, Lin SKS. The use of the Visual Analogue Scale for the assessment of labour pain: a systematic review. *JBI Database Syst Rev Implement* 2010;**8**:972–1015

80. Harvey S, Rach D, Stainton MC, et al. Evaluation of satisfaction with midwifery care.*Midwifery* 2002;**18**:260–267. http://dx.doi.org/10.1054/midw.2002.0317

81. Bublitz MH, Bourjeily G, D'Angelo C, et al. Maternal sleep quality and diurnal cortisol regulation over pregnancy. *Behav Sleep Med* 2018;**16**:282–293. https://doi.org/10.1080/15402002.2016.1210147

82. Larsson CA, Gullberg B, Råstam L, et al. Salivary cortisol differs with age and sex and shows inverse associations with WHR in Swedish women: a cross-sectional study. *BMC Endocr Disord* 2009;**9**:16.

83. Sundaram L, Swaminathan S, Ranjakumar T, et al. Intraocular pressure variation in pregnancy: a prospective study. *Int J Reprod Contracept Obstet Gynecol* 2017;**5**:1406–1409. http://dx.doi.org/10.18203/2320-1770.ijrcog20161294

84. Romano A, Tempesta B, Micioni Di Bonaventura MV. et al. From autism to eating disorders and more: the role of oxytocin in neuropsychiatric disorders. *Fron Neurosci* 2016;**9**:497. https://doi.org/10.3389/fnins.2015.00497

85. Uvnäs-Moberg K, Ekström-Bergström A, Berg M. et al. Maternal plasma levels of oxytocin during physiological childbirth–a systematic review with implications for uterine contractions and central actions of oxytocin. *BMC Pregnancy Childb* 2009;**19**:285.

86. Faul F, Erdfelder E, Lang AG, et al. G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007;**39**:175–191.

87. Snyder M, Wieland J. Complementary and alternative therapies : what is their place in the management of chronic pain ? *Nurs Clin North Am* 2003;38:495–508. http://dx.doi.org/10.1016/S0029-6465(02)00098-1

88. Sekhavat L, Behdad S. The effects of meperidine analgesia during labor on fetal heart rate. *Int J Biomed Sci* 2009;**5**:59.

89. Reynolds F. The effects of maternal labour analgesia on the fetus. *Best Pract Res Clin Obstet Gynaecol* 2010;**24**:289–302. https://doi.org/10.1016/j.bpobgyn.2009.11.003

90. Whitburn LY, Jones LE, Davey M, et al. The nature of labour pain : An updated review of the literature. *Women and Birth* 2018;32:28–38. http://dx.doi.org/10.1016/j.wombi.2018.03.004

91. Woo AK. Depression and Anxiety in Pain. *Br J Pain* 2010;4:8–12. https://doi.org/10.1177/204946371000400103

92. Turner JA, Deyo RA, Loeser JD, et al. The importance of placebo effects in pain treatment and research. *J Am Med Assoc* 1994;**271**:1609–1614. https://doi.org/10.1001/jama.1994.03510440069036

93. Brook CA, Schmidt LA. Social anxiety disorder: A review of environmental risk factors. *Neuropsychiatr Dis Treat* 2008;**4**:123–43.

Figure Legend

Figure 1 Mechanisms of action Reflexology therapy.

Figure 2 Mechanisms of action Massage therapy.

Figure 3 CONSORT flow diagram.

Figure 4 Research personnel training and responsibility matrix.

Figure 5 (a) shows the timeline of outcomes measurement in the intervention group; (b) shows the timeline of outcomes measurement in the control group.

Table Legend

Table 1 Steps of the Intervention.

Table 2 Summary of Primary Outcomes and Measurement Tools.

Table 3 Summary of Secondary Outcomes and Measurement Tools.

Table 1: Steps of the Intervention

Steps	Process
1.	Prepare the equipment.
2.	Explain the procedure to the primigravida & advise her to lay on her left side* with a pillow on the side of her stomach.
Breathing Exercise Intervention for 5 minutes	
3.	Ask the primigravida to perform deep breathing by inhaling slowly through the nose for two seconds and then consciously release the air by breathing out for another two seconds during contractions.
4.	Rest for 1–3 seconds, then repeat the same technique for a total of 5 minutes. Then proceed to the reflexology as described below.
Reflexology Intervention Technique for 10 minutes on each foot	
5.	Put a towel under the right foot and cover the left leg.
6.	Apply warm oil over the right foot and roll it left to right 5 times.
7.	Press palms on the Achilles heel and knead the ankle 5 times.
8.	Knead the thumb pads on the central and bottom parts of the heel 5 times.
9.	Knead the foot following the CIUW** shape on the lateral and intermediate aspects of the foot followed by the MST*** shape 5 times.
10.	Press the wooden reflexology stick on the toes, forefoot, mid-foot, and hind-foot 5 times.
11.	Repeat Steps 5–11 on the opposite side. Then proceed to the next lower limbs massage.
Lower Limbs Massage for 2 minutes 30 seconds on each leg	
12.	Effleurage massage on the whole, lower flexed leg by using two hands 3 times.
13.	Half effleurage massage from the heel to the popliteal area 3 times.
14.	Palm and thumb kneading on the gastrocnemius muscle over the lateral & medial sides, followed by scooping on the gastrocnemius, each step 3 times.
15.	Thumb kneading on the hamstring muscle over the medial, intermediate, and lateral sides 3 times.
16.	Repeat Steps 12–17 on the right leg. Then proceed to lower back massage.
Lower Back Massage for 15 minutes	
17.	Effleurage massage from the sacrum to the shoulders and deltoids 3 times.
18.	Thumb kneading & pressure over the lateral sides of the lumbar area of the spine 3 times.
19.	Apply fist knuckling motion and thumb kneading on the lower back, side by side, 3 times. Then proceed to upper back massage.

Upper Back Massage for 15 minutes	
20.	Effleurage massage followed by palm kneading from the lumbar region to trapezius laterally 3 times.
21.	Thumb kneading over both sides of erector spinae, then draining between the ribs towards the armpit areas 3 times.
22.	Apply squeeze on the deltoid muscle with draining towards the armpit 3 times.
23.	Apply finger kneading on trapezius muscle, followed by fist scooping 3 times.
24.	Finally, press on the neck and shoulder area on both sides 3 times.

* The left side position allows maximum blood flow to the placenta, because it applies less pressure from the foetus on the vena cava.[70]

**CIUW shape: C-shape; I-shape; U-shape, and W-shape. These shapes indicate the orientation and placement of the palms and knuckles of the therapist.

***MST shape: M-shape, S-shape, and T-shape. These shapes indicate the orientation and placement of the palms and knuckles of the therapist.

Table 2: Summary of Primary Outcomes and Measurement Tools

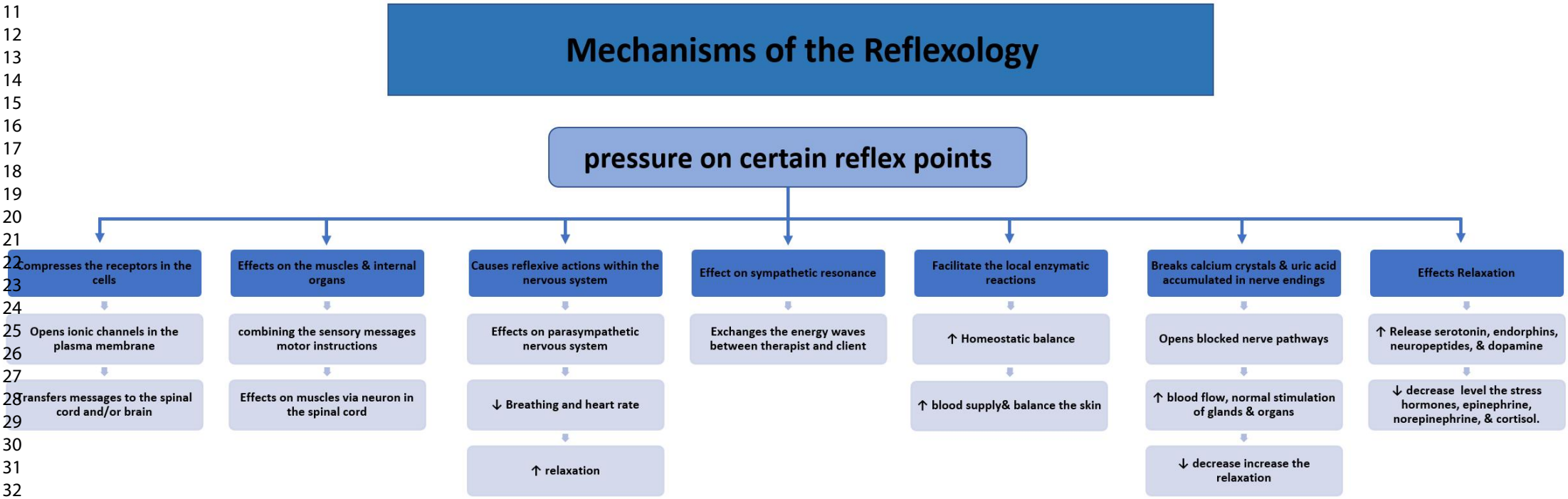
Primary Outcomes	Tools	Psychometric tests	Method of assessment
Pain	PBI	100% inter-rater reliability *r* coefficient was 0.45, 0.50, and 0.44 between PBI and PPI.[71,72]	Assessor-rated,[71] five-category behavioural observation scale
	VAS	Moderate correlation ($r = 0.54$) with the verbal rating and is considered valuable when mixed with other tools;[73,74] 0.97 intraclass correlation coefficient of 24 hours interval test-retest reliability.[75]	Self-reported VAS,[76] contains six different coloured parts anchored by two extremes of 'no pain' and excruciating pain to mark on the line-map by primigravidae.[77]
Anxiety	AASPWL	> 0.8 concordance test content validity index Kendall's W between the opinions of the experts (W= 0.090; *P*= 0.080) with Cronbach's alpha level of 0.77;[78] significantly correlated (*r*= 0.369) with the Beck Anxiety Scale.[78]	Questionnaire consists of nine items,[78] on a 5-point scale: the higher the mean score the higher the anxiety

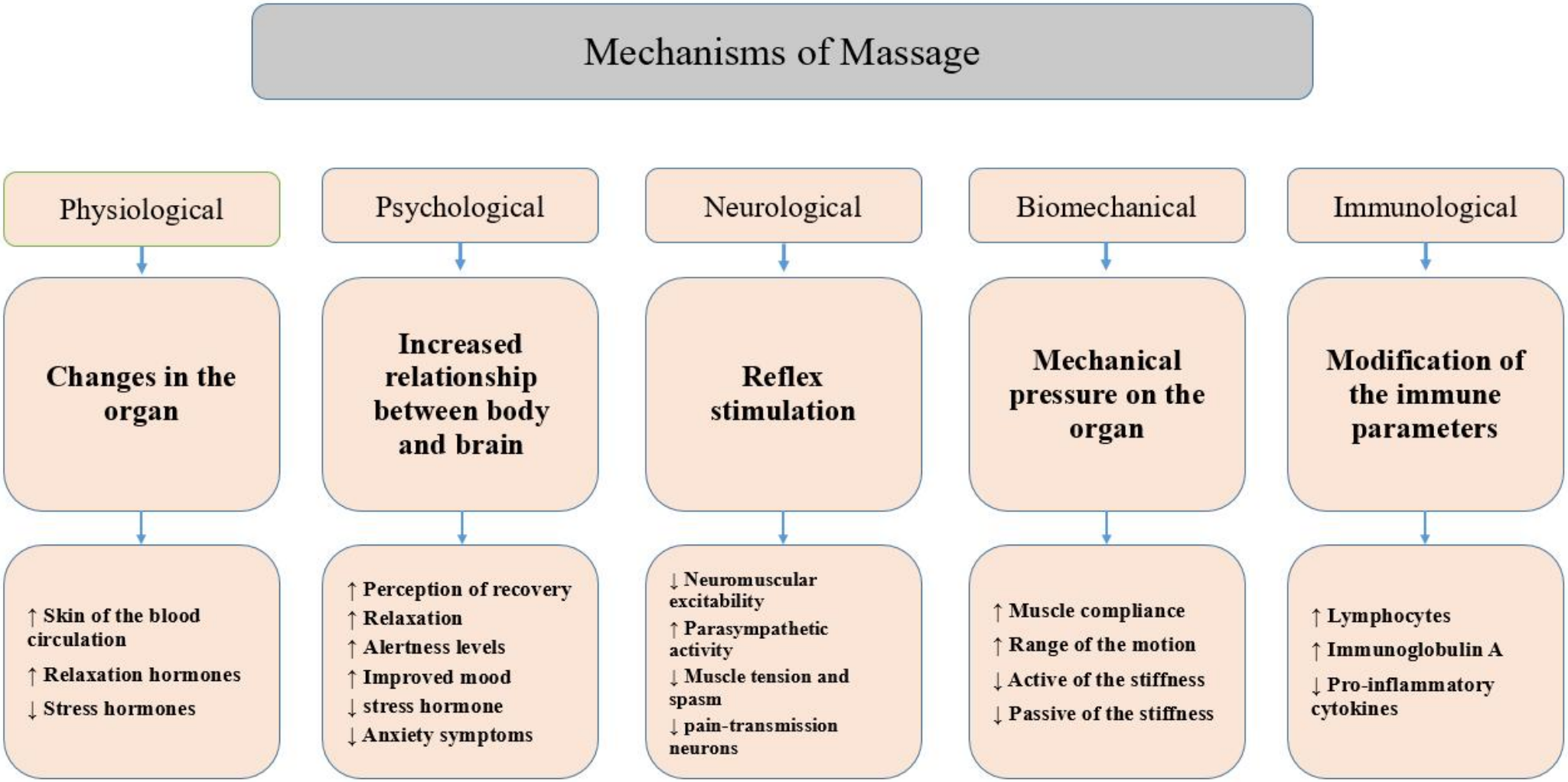
PBI= Present Behavioural Intensity; VAS= Visual Analog Scale; AASPWL= Anxiety Assessment Scale for Pregnant Women in Labour.

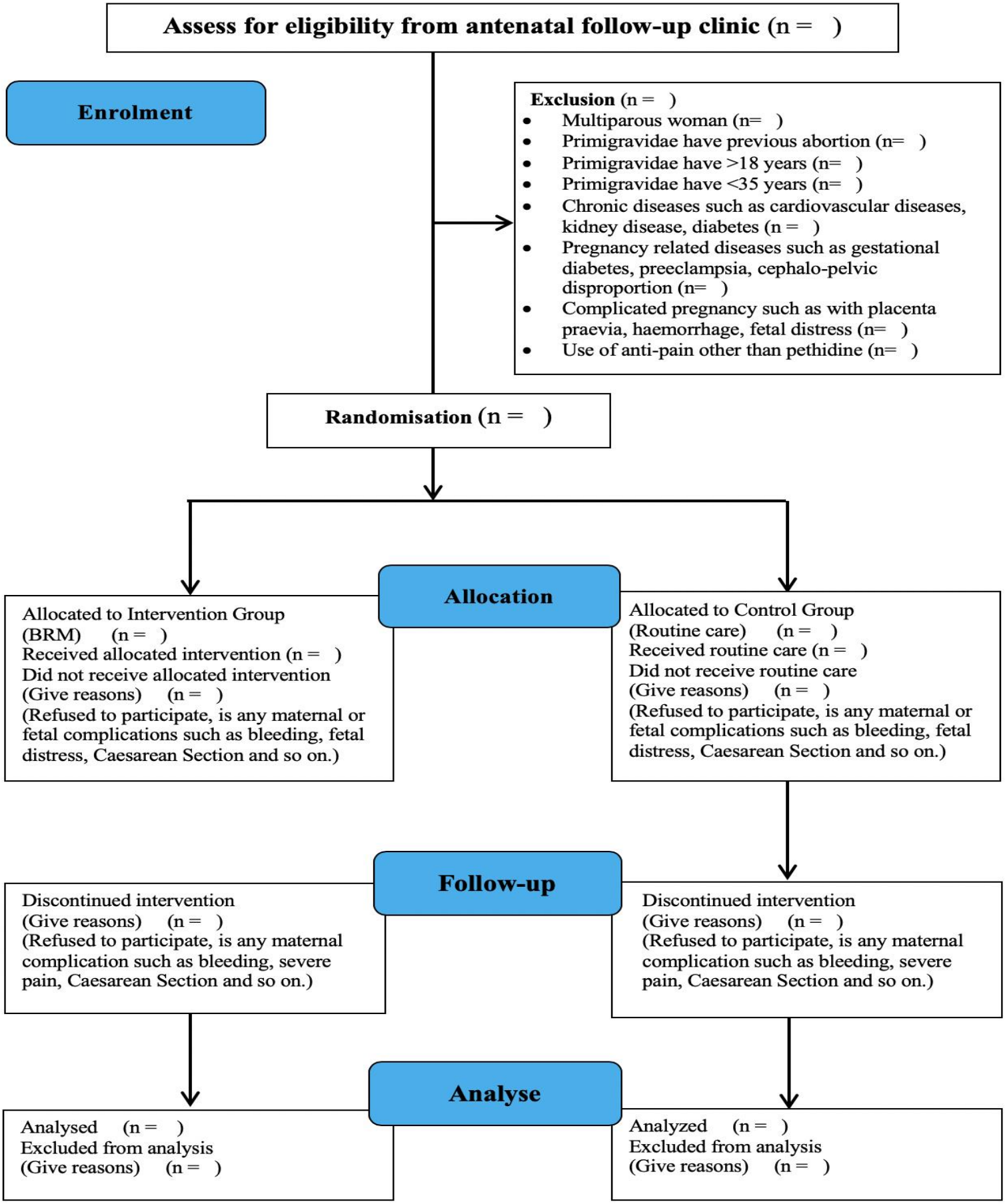
Table 3 Summary of Secondary Outcomes and Measurement Tools

Secondary outcomes	Measurement tools	Method of assessment
Maternal stress hormones level	Blood sample for ACTH, cortisol, oxytocin	Blood sample will be drawn from the median cubital vein during the insertion of IV cannula (routine care)
Maternal vital sign	Thermometer Sphygmomanometer	Recorded on the vital sign monitoring chart and cardiotocograph.
FHR	Cardiotocograph	Recorded on the vital sign monitoring chart, cardiotocograph chart, and partograph.
Duration of labour	Partograph	Partograph at two separate time intervals, a sum of labour duration from 3 to 6 cm of cervical dilatation and from 6 cm to delivery of the placenta
Neonatal Apgar score	Apgar score table	Taken from the delivery room medical record
Maternal satisfaction	Six Simple Questions.[80]	Self-reported 7-point scale (1-7) from "strongly disagree to "strongly agree" with higher scores signifying the higher level of satisfaction

ACTH= adrenocorticotropic hormone


Mechanisms of the Reflexology
pressure on certain reflex points
Compresses the receptors in the cells
Opens ionic channels in the plasma membrane
Transfers messages to the spinal cord and/or brain
Effects on the muscles & internal organs
combining the sensory messages motor instructions
Effects on muscles via neuron in the spinal cord
Causes reflexive actions within the nervous system
Effects on parasympathetic nervous system
↓ Breathing and heart rate
↑ relaxation
Effect on sympathetic resonance
Exchanges the energy waves between therapist and client
Facilitate the local enzymatic reactions
↑ Homeostatic balance
↑ blood supply& balance the skin
Breaks calcium crystals & uric acid accumulated in nerve endings
Opens blocked nerve pathways
↑ blood flow, normal stimulation of glands & organs
↓ decrease increase the relaxation
Effects Relaxation
↑ Release serotonin, endorphins, neuropeptides, & dopamine
↓ decrease level the stress hormones, epinephrine, norepinephrine, & cortisol.


Mechanisms of Massage
Physiological
Psychological
Neurological
Biomechanical
Immunological
Changes in the organ
Increased relationship between body and brain
Reflex stimulation
Mechanical pressure on the organ
Modification of the immune parameters
↑ Skin of the blood circulation
↑ Relaxation hormones
↓ Stress hormones
↑ Perception of recovery
↑ Relaxation
↑ Alertness levels
↑ Improved mood
↓ stress hormone
↓ Anxiety symptoms
↓ Neuromuscular excitability
↑ Parasympathetic activity
↓ Muscle tension and spasm
↓ pain-transmission neurons
↑ Muscle compliance
↑ Range of the motion
↓ Active of the stiffness
↓ Passive of the stiffness
↑ Lymphocytes
↑ Immunoglobulin A
↓ Pro-inflammatory cytokines


Assess for eligibility from antenatal follow-up clinic (n =)
Enrolment
Exclusion (n =)
Multiparous woman (n=)
Primigravidae have previous abortion (n=)
Primigravidae have >18 years (n=)
Primigravidae have <35 years (n=)
Chronic diseases such as cardiovascular diseases, kidney disease, diabetes (n =)
Pregnancy related diseases such as gestational diabetes, preeclampsia, cephalo-pelvic disproportion (n=)
Complicated pregnancy such as with placenta praevia, haemorrhage, fetal distress (n=)
Use of anti-pain other than pethidine (n=)
Randomisation (n =)
Allocation
Allocated to Intervention Group (BRM) (n =)
Received allocated intervention (n =)
Did not receive allocated intervention (Give reasons) (n =)
(Refused to participate, is any maternal or fetal complications such as bleeding, fetal distress, Caesarean Section and so on.)
Allocated to Control Group (Routine care) (n =)
Received routine care (n =)
Did not receive routine care (Give reasons) (n =)
(Refused to participate, is any maternal or fetal complications such as bleeding, fetal distress, Caesarean Section and so on.)
Follow-up
Discontinued intervention (Give reasons) (n =)
(Refused to participate, is any maternal complication such as bleeding, severe pain, Caesarean Section and so on.)
Discontinued intervention (Give reasons) (n =)
(Refused to participate, is any maternal complication such as bleeding, severe pain, Caesarean Section and so on.)
Analyse
Analysed (n =)
Excluded from analysis (Give reasons) (n =)
Analyzed (n =)
Excluded from analysis (Give reasons) (n =)

13 Research Assistants + 1 Principal Investigator

- Recruitment of nursing students who completed a 5-year nursing degree training and awaiting their job posting.
- Assigned to their preferred and suitable roles (coordinators, the outcome assessors, or massage therapists).
- One week training as research assistants in their respective roles.
- A pilot study to ensure their competency.
- Written study manual as a reference guide to be provided to all research assistants.

Research coordinators (4 pax.)	Outcome Assessors (4 pax.)	Massage therapists (5 pax.)
• Recruit eligible primigravidae at the antenatal clinic deliver brief health education on labour pain management at the antenatal clinic for 6 weeks. • Reassess the primigravidae women's consent and eligibility, • Allocate the women to either the intervention or control group. • Alert the massage therapists and outcome assessors when the cervical dilatation of the trial participant reaches 6 cm. • Distribute outcomes assessment record form to the outcome assessors. • Encode the questionnaire package according to the participant's allocated group. • Organise the entry sequence for the outcome assessors and the massage therapists to enter the delivery rooms according to the scheduled time.	• Assess and fill-up questionnaires: 1. Present behavioural Intensity (PBI). 2. Visual Analog Scale (VAS). 3. Anxiety Assessment Scale for primigravidae Women in labour (AASPWL), 4. Six Simple Questions (SSQ) for maternal satisfaction. • Retrieve the maternal vital signs, fetal heart rate, duration of labour, and neonatal Apgar score from the health records. • Record all the outcomes in the designated form.	• Perform breathing exercise, foot reflexology and back massage during labour (BRM). 1. Breathing exercise (5min). 2. Foot Reflexology (10 min on each foot), 3. Back massage (35min).

Sub-divided into two shifts per day to ensure all the eligible and consented primigravidae will be captured

Day Shift (9 am - 9pm)

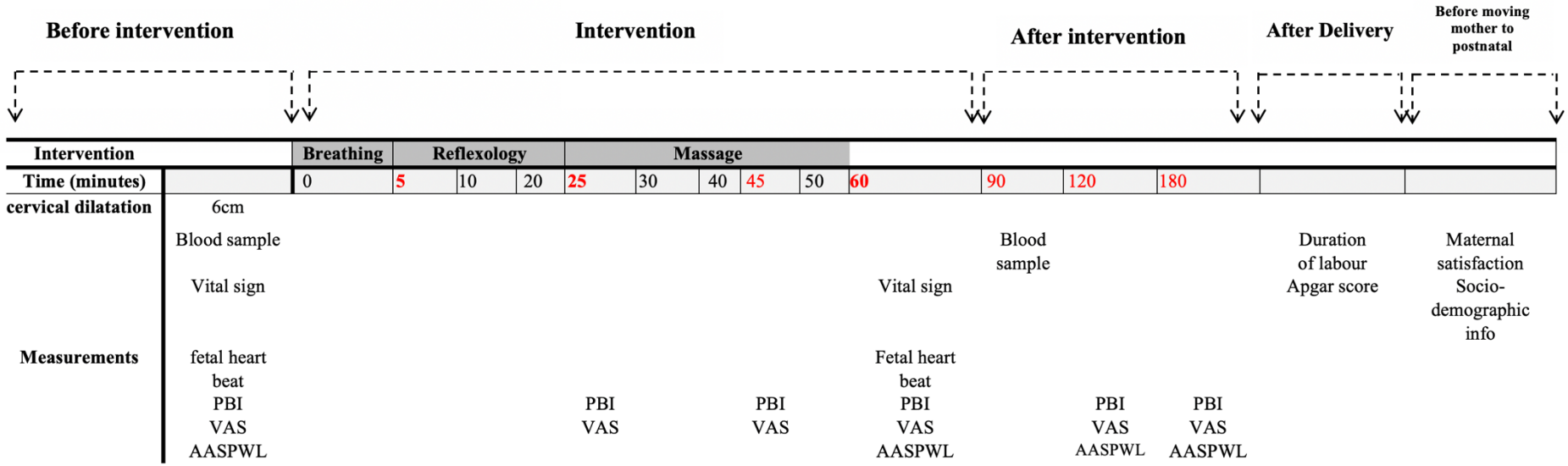
2 Coordinators, 3 Massage therapists, and 2 Outcome Assessors

Night Shift (9 pm - 9 am)

2 Coordinators, 2 Massage therapists, 2 Outcome Assessors, and Principal Investigator

a

Intervention Group



b

Control Group