COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY
YALE UNIVERSITY SCHOOL OF MEDICINE
YALE-NEW HAVEN HOSPITAL

Study Title: The Stimulation Therapy to Induce Mothers (STIM) Study
Nipple stimulation with an electronic breast pump for labor induction: A parallel-group randomized controlled trial

Principal Investigator (the person who is responsible for this research):
Moeun Son, MD, MSCI
Section of Maternal-Fetal Medicine
Department of Obstetrics, Gynecology, and Reproductive Sciences
Yale School of Medicine
333 Cedar Street
P.O. Box 208063
New Haven, CT 06520
Phone Number: 475-414-5328

Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to evaluate the use of nipple stimulation with the aid of an electric breast pump or by hand for induction of labor.
- Study procedures will include: You will be interviewed, and your medical record will be reviewed, for a basic history. The information collected is outlined in detail below. You will receive a standard manual cervical exam prior to induction of labor by your maternity care provider, followed by random assignment to either nipple stimulation by hand or with an electric breast pump (your choice) or standard exogenous oxytocin infusion. If assigned to nipple stimulation, you will receive a brief tutorial from a labor nurse or research staff. Participants in this group will be asked to keep a brief "diary" of their experience during labor. Participants in both groups will be assessed for pain during childbirth, and all participants will be asked to fill out several questionnaires, once during their postpartum hospital stay and once at 4-12 weeks postpartum via telephone and/or email.
- No additional healthcare visits are required.
- There are potentially some risks from participating in this study. There have been a few reports of fetal distress with electric breast pump use to induce uterine contractions, in one reported case requiring an urgent cesarean section delivery. It is important to recognize that uterine contractions and the labor process can naturally cause fetal distress, and the small prior studies that have compared breast pump use with oxytocin use during labor have not shown breast pump use to be more dangerous. You also may have some mild nipple or breast discomfort or soreness. You will have the option to discontinue breast pump use at any time if this occurs, or for any other reason.
- The study may have no benefits to you. However, we suspect that breast pump use may increase your sense of control during labor or your readiness for, or success with, breastfeeding. It may benefit other women by ultimately allowing a more individualized approach to induction of labor that prioritizes each woman's preferences and values for the childbirth process.

- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?

We are asking you to take part in a research study because **you are over 18 years of age, your gestational age is at least 36 weeks, your gestation is vertex-presenting (the fetal head is down), and you are planned to receive supplemental oxytocin for labor induction**. We are looking for **562** participants to be part of this research study.

Who is paying for the study?

This study is being funded in part by the Albert McKern Scholar Award awarded to the principal investigator.

What is the study about?

The purpose of this research study is to evaluate the use of nipple stimulation with an electronic breast pump (or by hand) pump for induction of labor. Induction of labor typically involves receiving an intravenous (IV) medication called Pitocin. Pitocin is currently considered the standard of care for induction of labor. Pitocin has the same function as a hormone called oxytocin, which your brain naturally produces at the end of pregnancy in order to bring on labor and birth. Nipple stimulation causes the body to produce more of this hormone. This study will evaluate whether nipple stimulation during the labor process can improve labor and delivery outcomes. We hope that this will ultimately allow a more individualized approach to induction of labor that prioritizes each woman's preferences and values for the childbirth process.

What are you asking me to do and how long will it take?

If you agree to take part in this study, this is what will happen:

You will be briefly interviewed, and your medical record will be reviewed, for the following information:

- Reason for induction of labor
- Demographic information: age, race, ethnicity, insurance status
- Medical history: first clinic weight, current weight, height, chronic disease history
- Obstetrical history including outcomes of any prior pregnancies
- Social history: marital status, educational level, alcohol use, and tobacco use
- Current pregnancy complications

The process will then begin with a manual exam of your cervix by your healthcare provider (as would be conducted prior to any induction of labor). You will then be randomly assigned to participate in usual induction of labor care or induction using nipple stimulation (electric or manual). Your chances of being assigned to either condition are equal.

Your treating obstetrician or midwife has decided that you will receive Pitocin for induction of labor as the current standard of care. You are being asked to agree to be randomized to either current standard of care (Pitocin) or to try nipple stimulation for inducing labor. If you are

randomized to nipple stimulation for inducing labor, Pitocin (standard of care) will always be available as a back-up if nipple stimulation does not adequately work.

If you are randomized to nipple stimulation, you will receive a 5-minute tutorial on the use of hand stimulation or use of the breast pump by a labor nurse or research staff. If you choose to use the breast pump, a hospital-grade breast pump (Medela Symphony® Breast Pump), the individual pump kit, and lanolin ointment will be provided to you. You may choose to use your own personal non-hospital breast pump and pump kit if you prefer. We ask that you maintain a "diary" during this process, which will describe the starts and stops in stimulation, the pump suction used, the transitions between breasts, and any additional notes you wish to make. Stimulation by hand or with the breast pump will be applied for no more than 30 minutes before alternating to your other breast. This will continue until contractions are adequate for labor progress (occurring at least every 3 minutes). If contractions become too frequent, the stimulation will be decreased, or the stimulation will be stopped. You may request a decrease in pump suction or a pause in stimulation at any time, but this pause should not exceed 30 minutes if the frequency of your contractions becomes less than every 3 minutes. We ask that you perform breast pump stimulation for a minimum of two hours. After at least two hours of breast pump stimulation, if there has been no cervical change or the desired contraction pattern is not achieved, your provider may recommend transition to synthetic oxytocin use (Pitocin). In addition, you may choose to cross over to Pitocin if you desire at any time, even before the recommended two hours of breast pump stimulation.

If you are randomized to exogenous oxytocin, oxytocin infusion will be initiated at the standard rate of 2 mU/min and will not exceed 20 mU/min. This will be done as part of your standard of care. Decisions to change the infusion rate are based on fetal status, contraction pattern, and maternal coping and any such changes will be in keeping with Yale-New Haven Hospital Department of Obstetrics, Gynecology, and Reproductive Sciences policy and will not be affected by your participation in this research.

Regardless of randomization group, your induction will not be considered to have "failed" until at least 12 hours have elapsed since both rupture of membranes and use of synthetic oxytocin. All participants will complete two questionnaires at enrollment to establish baseline: assessment of pain using the visual analog scale, and the Edinburgh Postnatal Depression Scale. During the hospital postpartum stay, all participants will be asked to assess the pain experienced during childbirth using the visual analog scale and asked about their intention to breastfeed , and to complete two questionnaires: the Labor Agentry Scale to assess feelings of control during childbirth, and the Birth Satisfaction Scale-Revised (BSS-R) to assess their satisfaction with the childbirth process. All participants will receive a phone call and/or email between 4 and 12 weeks postpartum to assess for any unanticipated office or hospital visits, and to complete the two additional questionnaires: the Maternal Breastfeeding Evaluation Scale (MBES)) to assess feelings about, and early experiences of, breastfeeding, and the Edinburgh Postnatal Depression Scale. Should your scores suggest an increased risk for depression, we will notify your primary obstetric provider/team and refer you to them for additional care.

What are the risks and discomforts of participating?

Oxytocin is naturally produced by the human body and is the most commonly used method of labor induction, which occurs in over a quarter of all pregnancies in the United States. Oxytocin should not be used in cases where labor and vaginal delivery are not considered safe.

Most commonly, oxytocin is well tolerated by the mother and fetus. The **most common** complication is excessive uterine contractions, which is called tachysystole and can cause fetal distress. This occurs in about 5 in 100 labor inductions with exogenous oxytocin administration. You will be monitored for signs of tachysystole during labor induction, and oxytocin infusion will be stopped if these signs develop. There are several **rare but serious** side effects to consider. Low sodium levels in the blood, which in severe cases is associated with headache, nausea, vomiting, abdominal pain, drowsiness, unconsciousness, seizures, and irreversible brain damage. Severe symptoms occur extremely rarely but have been reported. Lastly, low blood pressure can occur as it has been seen with very high doses of oxytocin administration, though it has never been reported as a side effect of the infusion protocol used at Yale-New Haven Hospital.

Endogenous oxytocin use via nipple stimulation has not been as heavily studied as exogenous oxytocin, which is why our study may yield important scientific advancement, but endogenous oxytocin use may also be associated with unknown risks as a result. There may be potential risks or inconveniences such as inadequate uterine contractions which may be consequently associated with prolonged labor. Similarly, like Pitocin, it is possible that nipple stimulation can cause excessive uterine contractions (tachysystole). You will be monitored for signs of tachysystole during labor induction, and nipple stimulation will be stopped if these signs develops. Research to date has shown no increased risk of cesarean section or other negative outcomes with the use of nipple stimulation compared to oxytocin infusion.

You may experience breast discomfort from the use of the breast pump. One study found that 1 in 6 women had nipple discomfort with the breast pump on a high suction setting that resolved with decreasing the suction, and no participants had skin damage or other injury to the nipple. If you experience discomfort during the study, you are able to pause your breast pump use at any time.

How will I know about new risks or important information about the study?
We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?
The benefits of using a nipple stimulation for labor induction are currently unproven. However, breast stimulation for labor induction may:

- Increase your sense of control or yield other improvements in your childbirth experience
- Decrease your risk of heavy vaginal bleeding (postpartum hemorrhage) after your delivery
- Improve your readiness for, or success with, breastfeeding, which in turn has substantial benefits to mothers and babies

How can the study possibly benefit other people?
This study may help determine if endogenous oxytocin (from your body, released via breast stimulation) outperforms exogenous oxytocin (synthetic) for the purposes of labor induction. Ultimately, this will allow a more individualized approach to induction of labor that prioritizes each woman's preferences and values for the childbirth process.

Are there any costs to participation?
If you take part in this study, you will not have to pay for any services, supplies, study procedures, or care that are provided for this research only (they are NOT part of your routine

medical care). However, there may be additional costs to you such as those costs associated with your hospital stay for labor induction, childbirth, and your postpartum period which will be billed to you and/or your insurance. You will be responsible for any co-payments required by your insurance. If you have no insurance, or your insurance refuses coverage for any part of your care, you will need to pay these costs.

Will I be paid for participation?

You will be paid up to a total of $20 if you complete all surveys that are part of this study. You will receive $10 if you complete all four study surveys during your hospital postpartum stay prior to discharge, and you will receive another $10 if you complete two additional study surveys at 4 to 12 weeks postpartum. You will receive these payments in the form of gift cards. We will use a Bank of America pre-paid debit card to provide the payment. We will have to share your name, address, and telephone number with Bank of America for ePayments. You will receive the cards in the mail. You will need to to activate the card over the phone. You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments. Payment is conditional on the completion of all study surveys.

You will also be gifted a hands-free breast pumping bra and cooler bag to keep if you are randomized to nipple stimulation.

What are my choices if I decide not to take part in this study?

Instead of participating in this study, you may elect to proceed with your usual care with your maternity care provider. As you were determined to be eligible for this study, this will likely include exogenous oxytocin use, but ultimately, your healthcare plan will be determined by you and your maternity care provider.

How will you keep my data safe and private?

We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if you we learn that you are hurting a child or an older person.

We will have your name and phone number only visible to two research staff members. Once we have contacted you by telephone and collected information about your delivery, we will remove your name and other identifiers. We will replace these with a code number. This deidentified information will then be kept in a password-protected database on a password-protected computer. These files will only be accessed by a small group of research staff. Information will be kept for 7 years.

Your consent form documents will be kept in a locked cabinet in our research office, accessible only by Yale Maternal-Fetal Medicine research staff.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we will ask you for your permission.

We will also share information about you with other researchers for future research, but we will not use your name or other identifiers. We will not ask you for any additional permission.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called “Protected Health Information.” It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for

research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- The entire research record and any medical records held by **Yale-New Haven Health** created from the start of your pregnancy and up to 3 months after delivery.
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research regarding:
    - Indication for labor induction
        - 39 weeks of gestation and greater and no other medical indication
        - Premature rupture of membranes
        - Maternal medical indication, such as pre-gestational diabetes, chronic hypertension,
        - Pregnancy indication, such as oligohydramnios, cholestasis of pregnancy, gestational diabetes, hypertensive disorders of pregnancy
    - Components of the modified Bishop score: cervical dilation, cervical length or effacement, and fetal station from digital cervical exam
    - Demographic information: age, race, ethnicity, insurance status
    - Medical history: first clinic weight, current weight, height, chronic disease history
    - Obstetrical history including outcome(s) of any prior pregnancies
    - Social history: marital status, educational level, alcohol use, and tobacco use
    - Current pregnancy complications

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The U.S. Food and Drug Administration (FDA) This is done so that the FDA can review information about device (Medela Symphony® Breast Pump) involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Principal Investigator of the study
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?
By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

What if I change my mind?
The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to **Moeun Son, MD** at: Yale School of Medicine, 333 Cedar Street, P.O. Box 208063, New Haven, CT 06520.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. If you withdraw from the study, we will clarify with you whether you wish to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which you previously gave consent, may continue. If you completely withdraw from the study, no new health information identifying you will be gathered after the date you withdraw unless we receive your permission to do so. Non-identifying information that has already been collected up until the point of your withdrawal may still be used and given to others to ensure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?
If you are injured while on study, seek treatment and contact the study doctor as soon as you are able.

Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up any of your legal rights by signing this form.

What if I want to refuse or end participation before the study is over?
Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

We would still treat you with standard therapy or, at your request, refer you to a clinic or doctor who can offer this treatment. Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary. For example, this may occur if you develop serious side effects while participating in the study.

What will happen with my data if I stop participating?

If you withdraw from the study, we will clarify with you whether you wish to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which you previously gave consent, may continue. If you completely withdraw from the study, no new health information identifying you will be gathered after the date you withdraw unless we receive your permission to do so.

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator at 475-414-5328.

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

A description of this clinical trial (NCTxxx) will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date