Informed Consent Form

Project Name: Labor Induction in Low-risk Women at 39 Weeks of Gestation to Reduce Cesarean Rate: A Pilot Randomized Trial in China
NCT number: NCT07082530
Version Date: June 4, 2025

Dear Participant:
Greetings! You are invited to participate in the study " Labor Induction in Low-risk Women at 39 Weeks of Gestation to Reduce Cesarean Rate: A Pilot Randomized Trial in China " which has been reviewed and approved by the Clinical Research Ethics Committee of Women's Hospital, School of Medicine, Zhejiang University.

This informed consent form will introduce the background, purpose, methods and content, expected duration, and expected number of participants of the study. Please read it carefully and make a careful decision on whether to participate. When the researcher explains and discusses the informed consent form with you, you can ask questions at any time and have the researcher explain anything you do not understand. You may discuss it with your family, friends, and doctor before making a decision.

Your participation in this study is entirely voluntary, and you may withdraw voluntarily after joining. Your decision will not affect your normal medical rights and treatment in our hospital.

1 Introduction

For full-term low-risk parturients with good maternal and fetal conditions, what is the optimal delivery gestational age? In 2018, the American ARRIVE cohort study first proved through a multicenter randomized controlled trial (RCT) that elective induction of labor at 39 weeks significantly reduces the cesarean section rate compared with expectant management, without increasing or decreasing the risk of other adverse perinatal outcomes (NEJM, 2018). This finding has promoted a shift in the childbirth model in the West—currently, about 30%-35% of deliveries in countries such as the UK, the US, and Australia are completed through induction of labor, and the average delivery gestational age has decreased to about 38.8 weeks.

In China's clinical practice, elective induction at 39 weeks and expectant management have become two common clinical choices. However, the applicability of this strategy in the Chinese population has not been verified by evidence-based medicine. Due to ethnic differences, different intrapartum management norms, and China's higher baseline cesarean section rate, directly applying the conclusions of ARRIVE studies may have limitations. Carrying out a RCT for the Chinese population will provide key evidence for formulating localized childbirth strategies.

This study first applies multi-omics technology to evaluate the health effects of childbirth timing, which can capture subtle physiological changes not detected by traditional clinical indicators and provide a new dimension for optimizing offspring health management. Previous studies have shown no significant difference in the growth and development and disease incidence of offspring between elective induction at 39 weeks and expectant management, but the subtle physiological changes have not been deeply explored. Umbilical cord blood proteomics and metabolomics can reflect the fetal intrauterine development, while the establishment of early gut microbiota may affect the long-term risk of metabolic diseases and allergic diseases in offspring. With the help of these

omics technologies, this study will analyze the subtle biological differences between the two groups, predict the long-term health status of offspring, provide a scientific basis for individualized early interventions (such as feeding strategies), so as to optimize offspring health management and reduce disease risks.

2 Research Purpose

You are invited to participate because you meet the following criteria: full-term, singleton pregnancy, low-risk, and planning vaginal delivery. This study aims to evaluate the difference in the impact of elective induction at 39 weeks and expectant management (waiting for spontaneous labor) on the cesarean section rate.

3 Procedures

If you agree to participate, you will be randomly assigned (randomly generated by a third-party computer) to one of the following groups between 38 weeks and 6 days and 39 weeks of gestation. Other medical decisions during childbirth will be made by the attending physician according to the actual clinical conditions.

39-week induction group
• Admitted to the hospital for induction between 39 weeks and 0 day to 39 weeks and 4 days • Your doctor will select an appropriate induction based on cervical maturity. If the cervix is immature, cervical ripening will be performed first. • Continuous fetal heart rate monitoring during induction.
Expectant management group
Continue routine antenatal care until admission under the following circumstances: • Spontaneous labor • Your doctor deems medical intervention necessary • Reaching 41 weeks of gestation

You may be required to provide a small number of biological samples during the time periods shown in the following table. The collection process is non-invasive and painless for you and the baby, and the collection process will not increase your costs.

Timing	**Biological samples**
Before delivery	Parturient: 6 vaginal secretion swabs, 1 tube of feces
After delivery	Newborn: birth meconium, residual umbilical cord blood from the placenta
1 or 2 days old	Newborn feces (after meconium has been expelled)
7 days old	Newborn feces, collected at home and delivered via express within 1 hour
6 weeks old	Infant feces, collected at home and delivered via express within 1 hour
6 months old	Infant feces, collected at home and delivered via express within 1 hour

Postpartum Follow-up until 6 months after delivery

The research doctor will:

- Review your and the newborn's hospitalization medical records (including delivery method, medication records, etc.)
- Ask you to answer questions about childbirth pain and offspring feeding after delivery

- Conduct a telephone follow-up on feeding information 7 days after delivery; express delivery to collect the baby's feces at home;
- Arrange for mother-infant re-examination in our hospital 6 weeks after delivery, complete the baby's growth and development assessment, answer questions about offspring feeding, and collect the baby's feces;
- Arrange for mother-infant re-examination in our hospital 6 months after delivery, complete the baby's growth and development assessment, answer questions about offspring feeding, and collect the baby's feces.

4 Eligibility Criteria

4.1 Inclusion Criteria

1. Age ⩾18 years.
2. Singleton pregnancy or twin pregnancy reduced to singleton before 14 weeks.
3. Gestational age of 38 weeks 6 days or 39 weeks 0 days at randomization.
4. Eligible for vaginal delivery with a desire for vaginal birth.
5. Reliable gestational age determination (confirmed by methods in Section 2.4.2).
6. Maternal and fetal conditions assessed as favorable by at least two senior obstetricians, with no indications requiring delivery before 41 weeks.
7. Ability to understand study information and provide informed consent.

4.2 Exclusion Criteria

1. First ultrasound estimate >13 weeks 6 days.
2. Planned induction before 41 weeks.
3. Planned cesarean delivery or contraindications to vaginal delivery.
4. Already delivered, in labor, or ruptured membranes at enrollment.
5. Placenta previa, vasa previa, placenta accreta, or placental abruption.
6. Contraindications to induction (e.g., cervical cancer, history of uterine rupture, genital tract malformations, abnormal fetal position, cord prolapse).
7. Active vaginal bleeding exceeding spotting.
8. History of cesarean delivery or uterine/cervical surgery.
9. Cervical cerclage during this pregnancy.
10. Maternal conditions not suitable for expectant management beyond 39 weeks (e.g., pregestational diabetes, gestational diabetes requiring insulin, hypertensive disorders, intrahepatic cholestasis of pregnancy).
11. Fetal conditions not suitable for expectant management beyond 39 weeks (e.g., fetal death, major anomalies, growth restriction, macrosomia, anemia, oligohydramnios, polyhydramnios).
12. Maternal infections or positive screenings for sexually transmitted pathogens or group B Streptococcus.
13. Planned delivery at a non-study facility.
14. Participation in another intervention study affecting delivery management.

4.3 Termination Criteria

You can withdraw at any time on your own initiative, or the research institution will terminate your participation in the following circumstances:

1. You need other treatments, or you do not comply with the research plan;
2. The study is terminated early;
3. Other special circumstances required by the ethics committee, such as the occurrence of serious adverse events.

5 Possible Risks and Preventive Measures

Induction of labor and expectant management are routine obstetric procedures and may be associated with various complications of routine childbirth, but they will not additionally increase the risk of childbirth. The collection of biological samples will also not increase risks: the collection of vaginal secretions will be carried out in conjunction with antenatal examinations. After the fetus is delivered and the umbilical cord is cut, the residual blood in the umbilical cord can be discarded, or collected for research donation or self-preservation. The collection of umbilical cord blood in this study is the same and will not affect the baby's health. Infant feces are generally discarded, and this study retains part of them for research, which will not cause any impact on the baby.

6 Benefits

The treatment itself may not bring direct benefits to you and the fetus, but this study will provide your baby with a professional and comprehensive physical development assessment, including two additional free professional cognitive assessments, and the assessment results will be informed to you, which can screen for early neurodevelopmental disorders. In addition, on the basis of the routine 42-day re-examination, we will provide a free additional 6-month examination.

The omics analysis results of gut microbiota and umbilical cord blood can respectively reflect the baby's gut microbiota development status and trace back the intrauterine development situation, which can to a certain extent reflect the baby's future metabolic characteristics and other conditions. We will not charge you for the omics analysis, and the analysis results can help you adjust the feeding plan.

The medical data you and your baby provide for this study will help the medical community establish the standard for the optimal childbirth timing.

7 Alternative Procedures

The alternative plan is not to participate in this study and receive the current routine expectant management plan (waiting for spontaneous labor or induction of labor for medical indications).

8 Costs and Compensation

- Routine diagnostic and treatment procedures during childbirth and hospitalization, as well as routine 42-day postpartum re-examination items, are borne by medical insurance or individuals;
- Research-related additional examinations are free of charge, including 6-month mother-infant re-examination, professional pediatric scale assessment, etc.
- Biological omics analysis is free of charge, including sample collection, preservation, and analysis.

9 Confidentiality

If you decide to participate in this study, your participation and personal data in the study are confidential. Your research-related materials (biological specimens, questionnaires, etc.) will be identified by a study number rather than your name. Information that can identify your identity will not be disclosed to members outside the research team unless you give permission. All research members and the study sponsor are required to keep your identity confidential. To ensure that the study is conducted as specified, government regulatory authorities or members of the ethics committee may, as required, review your personal data at the research unit. When the results of this study are published, no personal information about you will be disclosed.

10 Principle of Voluntariness

Whether to participate in the study depends entirely on your will. You may choose not to participate in this study, or you may notify the researcher at any time to withdraw from the study. Your data will not be included in the study results, and your medical treatment and rights will not be affected in any way.

For your best interests, if you need other treatments, or you do not comply with the research plan, or a loss related to the study occurs, or there are other reasons that may affect the progress of the study, the doctor or researcher may terminate your continued participation in the study during the research process.

11 Participant Responsibilities

Provide true information about your own medical history and current physical condition; inform the research doctor of any discomfort you experience during this study; inform the research doctor whether you have participated in other studies recently or are currently participating in other studies.

12 Contact Information

During the study, if you have any questions or do not understand anything related to this study, you can always raise them to the responsible research doctor. Responsible Doctor: Gao Huajing, Contact Phone: 18867114750. If there is any important new information during the study that may affect your willingness to continue participating in the study, your doctor will notify you in a timely manner.

If you have any questions about your rights, please contact the Clinical Research Ethics Committee of Women's Hospital, School of Medicine, Zhejiang University, Contact Phone: 0571-89998819.

INFORMED CONSENT FORM

Signature Page

Consent Statement

I have carefully read this informed consent form, and I have had the opportunity to ask questions, all of which have been answered. My participation in this study is voluntary. I may choose not to participate in this study, or withdraw at any time after notifying the researcher without discrimination or retaliation, and my medical treatment and rights will not be affected in any way.

If I need other diagnoses/treatments, or I do not comply with the trial plan, or there are other reasonable reasons, the researcher may terminate my continued participation in this clinical study.

I will receive a signed copy of the "Informed Consent Form."

Subject's Name: _____

Subject's Signature: _____

Contact Information: _____

Date: _____ Year _____ Month _____ Day

If the subject is unable to read the informed consent form (such as an illiterate subject), a witness shall witness the informed process and sign.

Witness's Name (Print): _____

Witness's Signature: _____

Contact Information: _____

Date: _____ Year _____ Month _____ Day

Investigator's Statement

I have accurately informed the subject of the contents of the informed consent form and answered the subject's questions. The subject voluntarily participates in this clinical study.

Investigator's Name (Print): _____

Investigator's Signature: _____

Contact Information: _____

Date: _____ Year _____ Month _____ Day