

Official Title:
Immediate Postplacental Intrauterine Device insertion in high-risk patients

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1. Background

Approximately half of all pregnancies in the United States are unintended.¹ With the transition to new parenthood, women in the postpartum period are particularly susceptible to unintended pregnancy. Recent data has shown that among women 18-24 years of age, 57% had a repeat pregnancy within 18 months of delivery.²

Intrauterine devices (IUD) provide safe, effective, and long acting reversible contraception (LARC). For those who desire an IUD after delivery, common practice in the United States is insertion at 6 weeks postpartum. However, women who plan an IUD often face barriers to receiving one for many reasons including loss of insurance coverage, difficulty getting to postpartum visits, and early repeat pregnancy.³ Immediate postplacental IUD insertion is defined as IUD insertion within 10 minutes of the expulsion of the placenta.⁴ Although this practice is common in developing countries, it is rare in the United States. There are several potential advantages to immediate IUD insertion including the cervix is already dilated, postplacental insertion is often performed under labor anesthesia therefore patients can avoid the potential discomfort related to IUD insertion, in addition, no additional visit is needed.

Both the levonorgestrel and copper IUD provide contraception without interfering with breastfeeding.⁵ For women with limited access to medical care, hospitalization for delivery provides a unique opportunity to address the need for contraception. The major disadvantage to postplacental placement is an increase in expulsion rates; as high as 8-24% by 6 months.⁶ One study suggests that the rate of expulsion has to do with the insertion technique and provider experience.^{6,7} Despite this higher expulsion rate, continuation rates for IUD use at 6 months appear to be equivalent for postplacental IUD as compared to routine 6 week insertion.⁶ In a setting where women typically attend a postpartum follow-up visit where IUDs are routinely available, postplacental placement has not been shown result in higher uptake of IUDs or to be cost-efficient.⁶ However, in a population at high risk for lack of postpartum follow-up, the higher expulsion risk becomes less a concern, as the alternative to postplacental placement would be nonuse of contraception or use of a less effective method. ***Identification of a group of postpartum women at high risk for poor follow-up would enable targeted delivery of postplacental placement.*** Recent studies at our institution have shown women with a history of poor attendance to prenatal appointments are at high risk of not returning for routine postpartum IUD placement.^{8,9} Based on these recent studies, *we hypothesize that women with less than 10 prenatal visits or 2 or more no show visits who receive an immediate postplacental IUD will have higher rates of IUD continuation at 3 months than women who are scheduled to receive an IUD at a delayed postpartum visit.*

2. Study Objective: To determine whether immediate postplacental IUD placement will improve IUD uptake at 3 month postpartum in women with a history of poor prenatal clinic attendance.

3. Study Design:

The study will be a randomized clinical trial. Women with less than 10 prenatal visits and/or 2 or more no show visits who desire an IUD will be considered for enrollment. If consented and meet inclusion criteria, they will be randomized after delivery to receive an IUD immediately postplacental or at their routine postpartum visit.

Women who plan to deliver a live birth singleton via vaginal or cesarean delivery at OHSU hospital will be considered for inclusion in the study. Women who desire an IUD for postpartum contraception will be approached for study participation. The postpartum contraception plan is routinely documented during their prenatal course. It is also addressed by the obstetrical team upon admission to Labor & Delivery at OHSU. The obstetrical team will identify subjects who present in labor who meet the criteria of poor prenatal clinic attendance and express interest in intrauterine contraception. These women will be provided with information about the study, and if interested will be provided with informed consent counseling. Completion of the informed consent process and signing of the consent can be done before or after delivery depending on the individual circumstances of the labor. Subjects that meet all inclusion and no exclusion criteria, and agree to the terms of the study, will be entered into the study after a discussion of study procedures and signing the informed consent. Immediately after vaginal or cesarean delivery, consenting subjects will be randomized to immediate postplacental IUD placement or IUD placement at their routine postpartum visit. Women randomized to the immediate postplacental IUD group will receive their IUD within 60 minutes of placental delivery. To minimize interference with the early postpartum interval, all subjects will be asked to complete a demographic questionnaire at their convenience at some point prior to hospital discharge. Prior to discharge from the hospital women who received a postplacental IUD will be assisted in scheduling a routine postpartum visit with their primary provider. Subjects who are randomized for IUD insertion at their postpartum visit will be assisted in scheduling a postpartum visit and IUD placement with their usual obstetrical care provider. All subjects in the delayed group will be provided with contact information for the Women's Health Research Unit at OHSU. If a subject cannot obtain an IUD at her usual place of care, the device will be placed at no cost through the WHRU.

At 3 months after delivery, all subjects will be contacted by phone, text, or email to complete a questionnaire to determine whether they have had a known expulsion, pregnancy, or elective IUD removal. The questionnaire will include questions regarding ease of placement and overall satisfaction with the timing of placement. Subjects will be compensated for their participation in the study after the 3 month contact.

4. Subject Recruitment: Participants will be recruited upon admission to OHSU Labor and Delivery. Researchers will pre-screen eligible subjects based on eligibility criteria through EPIC medical records and collect demographic information from women who elect to enroll in the study. Women who desire an IUD and have a history of poor

prenatal clinic attendance with income <300% of the federal poverty line will be approached by residents. Subjects will be selected for the study according to the selection criteria detailed below.

5. Consent: Whenever feasible the information about this research project will be made available to patients prior to labor. Due to the nature of the study consent may be obtained during labor or in the immediate postpartum period. In order to ensure adequate consent is obtained in patients who present in labor, patients will be asked if it is an appropriate time to discuss a research study regarding timing of IUD placement. If the time is not appropriate the investigator will wait until the circumstances have changed to re-visit the research study. Whenever possible research investigators will discuss the proposed research and obtain informed consent in the presence of one of the patient's independent labor support persons. Patients will not be approached for participation in the study until at least 1 hour has passed after administration of systemic opioids or sedative medications. If feasible it may be preferable to delay approaching a patient until after epidural placement if such analgesia is desired by the patient as studies have shown that epidural analgesia does not alter mental status. Consent will always be obtained in the patient's primary language.

It is important to emphasize that consent prior to admission on labor and delivery is not possible, as we are seeking to enroll a group of women who have poor attendance at prenatal clinics. While there are many reasonable concerns around obtaining consent in labor, the investigators in this study will be physicians who are experienced with the consent process for medical and surgical procedures (including the placement of IUDs immediate postplacental). These physicians routinely obtain consent on the L&D unit, and understand the dynamics and unique challenges of laboring women. We have built in additional flexibility to have potential subjects complete the informed consent process after delivery.

6. Study Duration: The total duration for the study for each participant is expected to be approximately 3 months.

7. Number of Subjects and Statistical Power: The study is expected to enroll 50 female subjects. With the proposed sample size of 20 subjects in each group, the study will have power of 81% to yield a statistically significant result. This computation assumes that a 40% difference in the primary outcome of proportion of subjects using an IUD at 3 months of follow-up (corresponding to proportions of 0.9 versus 0.5). This effect size is estimated assuming 90% IUD continuation rate in the immediate IUD group which takes into account the high expulsion rate, as compared to a 50% IUD continuation rate in the delayed IUD group which corresponds to the rate of return seen in this population as supported in two prior studies conducted at OHSU^{8,9}.

8. Selection of Subjects:

a. Inclusion criteria:

- i. Female
- ii. 18 yo or older
- iii. Singleton pregnancy at ≥ 32 weeks gestation at time of enrollment

- iv. Voluntarily requesting either copper T380A or levonorgestrel IUD placement for postpartum contraception
 - v. English or Spanish speaking
 - vi. Able to give consent and agree to the terms of the study
 - vii. Less than 10 prenatal visits or 2 or more no show visits
 - viii. Since IUDs are not on our hospital formulary, the patient must qualify for a LARC IUD (this includes all Oregon Health Plan (OHP) or Citizen/Alien Waived Emergent Medical (CAWEM) insured patients or women with income <300% of the federal poverty line).
- b. Exclusion Criteria:
- i. Anatomic uterine abnormalities that prevent proper fundal placement of IUD (obstructive myomata, bicornuate, septate, etc)
 - ii. Chorioamnionitis (also consider other risk factors such as prolonged rupture of membranes >18 hours, prolonged labor >24 hours, fever >38C)
 - iii. Puerperal sepsis
 - iv. Unresolved postpartum hemorrhage
 - v. Extensive genital trauma
 - vi. Current incarceration
 - vii. Known or suspected untreated endocervical gonorrhea, chlamydia
 - viii. Wilson's disease, copper allergy (Paragard only)
 - ix. Known or suspected cervical or endometrial cancer or pelvic tuberculosis
 - x. Current breast cancer (LNG-IUS only)
 - xi. SLE with severe thrombocytopenia (Paragard only)
 - xii. Trophoblastic disease (benign or malignant)
 - xiii. AIDS not stable on antiretroviral

9. Treatment Allocation: Randomization will be accomplished by opening the next in a series of numbered sealed opaque envelopes. The envelope will contain the subject randomization assignment. The envelope will be opened immediately after delivery. The randomization scheme will be by computer block randomization.

10. Study Medications: All of the study medications are FDA-approved and they will be used according to the labeling indications.

a. The **levonorgestrel intrauterine system (Mirena® IUS)** is a radio-opaque T-shaped polyethylene device containing 52mg of levonorgestrel dispersed in polydimethylsiloxane on its stem. The progestin is released at a rate of 15 mcg per day. It is FDA approved for up to five years of use in the United States.

b. The **Copper T380A IUD (ParaGard®)** is a T-shaped polyethylene device with 380 mm² of exposed surface area of fine copper wire wound around its arms and stem. Barium sulfate has been added to the polyethylene frame to make the device radio-opaque. A 3-mm plastic ball is located at the base of the IUD, through which the polyethylene monofilament string passes. It is FDA approved for up to 10 years of use in the United States.

11. Study Laboratory Tests and Procedures:

a. Laboratory testing: No routine laboratory tests are indicated for the study. For immediate postplacental placement, no testing is indicated. For women randomized to IUD placement at their routine postpartum visit, clinicians will obtain urine pregnancy tests and or DNA probe for gonorrhea and chlamydia testing according to established clinic protocols. Should the test result be positive, the subject will be contacted by her primary provider for treatment.

b. Immediate postplacental IUD insertion technique: IUD insertion will be performed by an experienced study investigator (residents or faculty) who has received training in the technique. Pain management will be per clinical judgment and include pre-existing epidural/spinal, IV, or local anesthetic as necessary to ease comfort. Two ring forceps, ovum forceps, speculum/vaginal retractor, 4x4sponges, antiseptic solution, and the IUD will be added to the delivery table. Ultrasound will be available at the bedside. The external genitalia will be cleansed and properly draped. A speculum or vaginal retractor will be placed to visualize the cervix. The cervix will be cleansed with antiseptic and grasped at the anterior cervical lip with the ring forceps. The Cu IUD will be grasped with the ring/ovum forceps and placed at the uterine fundus. The Mirena can be placed with the IUD inserter, or with the forceps according the providers discretion. Ultrasound will be used to ensure fundal placement. At the end of insertion the IUD strings will be examined and cut flush with the external os. In subjects post-cesarean, the IUD will be placed either manually, with ring forceps, or the Mirena inserter, to the uterine fundus. Care will be taken to avoid incorporation of IUD strings into the hysterotomy closure. If the IUD becomes dislodged during placement, the IUD will be removed and reinserted to the uterine fundus using sterile technique.

c. Office IUD insertion: All insertions will be done according to the standard operating procedure at each clinic. A variety of usual care providers will provide the device, and the placement is outside of the study procedure. An exception will be subjects unable to obtain a device through their usual clinic. These women may obtain a device through an investigator at Women's Health Research Clinic. All study investigators will undergo review of manufacturer instructions. Pain management will be per clinical judgment and includes either no treatment, 1% lidocaine gel applied directly to the cervix with a cotton swab, or 1-2 mL of 1% lidocaine injected into the cervix prior to tenaculum placement. No paracervical block will be used unless clinically indicated. Dilation will be used if necessary. The IUD will be placed following FDA approved manufacturer instructions.

12. Study Visits

a. Screening: Pregnant women with a history of poor prenatal clinic attendance and OHP or CAWEM insurance who have identified IUD as their planned form of contraception will be approached upon admission to OHSU Labor and Delivery by a study investigator. After a description of the study and confirmation of their intent for IUD, informed consent will be obtained, screening for study inclusion criteria will be performed, and the initial questionnaire will be administered if possible. Release of information will be signed including the subjects contact information so that they can be contacted at 3 months postpartum as detailed below.

- i. Subject screening
- ii. Informed Consent
- iii. Release of information

- iv. Initial Questionnaire
- vi. Privacy Practices Information
- vii. Study Stipend Paperwork
- b. Randomization: Immediately after delivery the study subject randomization will be performed using sequential opaque envelopes. The subject will be informed of her group allocation and the study procedure will be reviewed. For participants randomized to insertion at their postpartum visit, an appointment will be scheduled with their primary provider prior to hospital discharge. If they are unable to obtain an IUD from their primary clinic, they will be given information to arrange IUD insertion at the OHSU Women's Health Research Unit. While placement at the WHRU is not "real world", we feel that it this follow-up is ethically justified to provide the same option to all participants for a no cost IUD regardless of randomization group.
 - i. Randomization revealed
 - ii. Schedule follow up appointment if needed
- c. IUD placement(IUD insertion – postplacental or postpartum visit): Prior to IUD insertion, the provider will discuss informed consent with the patient and will sign a formal surgical consent form to be placed in the patient's medical chart. The IUD will be inserted as detailed in study procedures. Subjects receiving postplacental IUDs will be encouraged to have the IUD strings checked at their postpartum visit by their primary provider. All subjects will be counseled on how to check their IUD strings.
 - i. IUD insertion procedure
- d. Follow Up: At three months postpartum, participants will be contact by phone, text, or email. They will be asked whether they have had a known expulsion, pregnancy, or elective IUD removal. A brief questionnaire will include questions regarding ease of placement and overall satisfaction with the timing of placement. A study stipend will be provided at this time. Participants who did not follow up for IUD insertion or those that report IUD expulsion will be encouraged to contact their primary provider to discuss contraception. Chart review for confirmation of IUD placement will be performed.
 - i. Final questionnaire
 - ii. Study subject stipend paperwork

13. Data Analysis: Data will be validated and entered into a computer. Statistical analysis will be carried out using STATA. Principal outcome measures include pregnancy and removal rates, cumulative expulsion, and continuation rates.

14. Data management: All patient data sheets will be kept confidential and in a locked office. A unique patient study identification number will be placed on the data forms. Study identification will be subject last initial and a unique three digit identifier. No subject names will be included with the study data. Study identifiers kept in a logbook will be assigned to each patient to protect confidentiality. For subjects who do not enroll, all screening documents will be kept in a locked office and password protected computer and confidentially destroyed once study is complete. When undergoing statistical analysis, the forms will be transferred to the primary investigator's locked office. Patient identifiers will be stored separately from the data files on the primary investigator's password-protected computer. Only the study investigators will have access to this identifier list.

15. Compensation and costs for participation: All IUDs will be covered by the LARC program (a philanthropic program that provides no cost devices to women meeting eligibility criteria) or their Oregon Health Plan insurance. Subjects will be compensated \$50 at the conclusion of the study after completion of the three month follow up phone call.

16. Withdrawal: Subjects will have the right to withdraw from the trial at any time on their own request for any reason. The reason for withdrawal will be recorded in detail. Subject who choose to withdrawal from the study will be contacted for follow up to complete the three-month follow up questionnaire. Additionally, any data obtained up to the point of withdrawal will be analyzed in accordance with intention to treat.

17. Non-English speaking participants: Consent forms will be translated into Spanish by a certified interpreter. Telephone calls to subjects will be completed with the assistance of a certified OHSU interpreter.

18. References

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