Study Title: A randomized controlled trial of ultrasound guided IUD insertion
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PennState

HRP-591 - Protocol for Human Subject Research

Protocol Title:

A randomized controlled trial of ultrasound guided IUD insertion

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Clinicaltrials.gov Registration #:

NCT03493815

Important Instructions for Using This Protocol Template:

1. Add this completed protocol template to your study in CATS IRB (http://irb.psu.edu) on the "Basic Information" page, item 7.
2. This template is provided to help investigators prepare a protocol that includes the necessary information needed by the IRB to determine whether a study meets all applicable criteria for approval.
3. **Type your protocol responses below the gray instructional boxes of guidance language. If the section or item is not applicable, indicate not applicable.**
4. **For research being conducted at Penn State Hershey or by Penn State Hershey researchers only, delete the instructional boxes from the final version of the protocol prior to upload to CATS IRB (http://irb.psu.edu). For all other research, do not delete the instructional boxes from the final version of the protocol.**
5. When making revisions to this protocol as requested by the IRB, please follow the instructions outlined in the Study Submission Guide available in the Help Center in CATS IRB (http://irb.psu.edu) for using track changes.

If you need help…	
University Park and other campuses: Office for Research Protections Human Research Protection Program The 330 Building, Suite 205 University Park, PA 16802-7014 Phone: 814-865-1775 Fax: 814-863-8699 Email: irb-orp@psu.edu	**College of Medicine and Hershey Medical Center:** Human Subjects Protection Office 90 Hope Drive, Mail Code A115, P.O. Box 855 Hershey, PA 17033 (Physical Office Location: Academic Support Building Room 1140) Phone: 717-531-5687 Fax number: 717-531-3937 Email: irb-hspo@psu.edu

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1.0 Objectives

1.1 Study Objectives

Blind procedures are basic to the practice of obstetrics and gynecology and often require substantial experience to master. Ultrasound is increasingly used to guide uterine procedures that have traditionally been performed blindly such as embryo transfer. Currently there are limited prospective trials for studying the utility of ultrasound guidance for many other procedures. Our objective is to determine the utility of ultrasound-guided intrauterine device (IUD) insertion compared to traditional blind insertion at an academic health institute where skill level of provider can vary greatly. The subject and her clinician will determine which type of IUD they will receive and all types of IUD's (copper and progesterone containing) will be acceptable for participation in the study. Our hypothesis is that transabdominal ultrasound guided insertion will lead to lower discontinuation rates and greater patient satisfaction.

1.2 Primary Study Endpoints

IUD discontinuation rate at 6 months

1.3 Secondary Study Endpoints

Malposition rate at the time of 4-6 week post insertion string check
Pain during insertion as determined by the visual analog scale (VAS)
Satisfaction at 6 months determined by categorical assessment and rate of side effects as reported by patient

2.0 Background

2.1 Scientific Background and Gaps

Blind procedures are basic to the practice of obstetrics and gynecology, but often require substantial experience to master. Ultrasound is increasingly used to guide uterine procedures that traditionally have been performed blindly such as embryo transfer. Currently, there is one small randomized trial that studied malposition rates 1 week following IUD insertion with ultrasound guidance compared to blind insertion and found promising data to support use of US guidance [1]. However, that trial is limited in its small sample size of 40 per arm and short follow up of 1 week. There still is paucity of information on the effect of ultrasound guidance on long term discontinuation rate, complications, and satisfaction compared to blind insertion.

2.2 Previous Data

There are no preliminary data at this time

2.3 Study Rationale

Our goal is to determine the utility of ultrasound guided IUD insertion compared to the traditional blind insertion at an academic health institute where the skill level of the provider can vary greatly. We hypothesize that ultrasound-guided insertion will lead lower IUD discontinuation rates and greater patient satisfaction.

3.0 Inclusion and Exclusion Criteria

3.1 Inclusion Criteria

1. Female >18 years of age undergoing IUD insertion in an office setting
2. Fluent in spoken and written English
3. Premenopausal

3.2 Exclusion Criteria

1. Less than 6weeks postpartum at time of IUD insertion
2. Intraoperative IUD insertion
3. Pregnant
4. Prisoners
5. Cognitive impairment
6. unable to read or write

3.3 Early Withdrawal of Subjects

3.3.1 Criteria for removal from study

- Subject withdraws consent
- A decision by the investigator to withdraw subject due to safety reasons

3.3.2 Follow-up for withdrawn subjects

Subjects who withdraw prior to IUD insertion will not receive the intervention and will not receive any research related follow up, they will receive routine follow up as directed by their physician.
Subjects who withdraw after the IUD insertion will still receive their routine care 4-6 week string check follow up but will not have the concominent research ultrasound to check positioning of IUD.
Those who withdraw after IUD insertion will also not have a 6-month clinic follow up visit for string check and satisfaction Likert scale completion.

4.0 Recruitment Methods

4.1 Identification of subjects

Participants will be identified in several ways:

- By the PI/SI during a patient clinic visit
  - The study team may also review the investigator's and coinvestigator's clinic schedules for patients who are scheduled for an IUD insertion. If subjects are not identified during a clinic visit and given the information they will be contacted by the study coordinator to see if they are interested and the study coordinator will explain the study and send them the consent form to review before their IUD insertion appointment. If the study coordinator is unable to reach the subjects, a letter from the PI and a copy of the ICF will be mailed to the patient's

home address. The letter provides contact information for the study coordinator and co-PI so the patient can call or email with any questions prior to their appointment.

4.2 Recruitment process

Women will be given information on the study at the time of scheduling for the IUD insertion clinic appointment, either in the clinic appointment when she is considering IUD or inpatient for those considering an IUD postpartum (greater than 6 weeks after delivery). Eligibility will be determined by the investigator and women who are eligible will be given information about the study by the investigator. They will have the opportunity to ask questions and if they are interested in participating they will be given a copy of the consent form to take home and read. Upon arrival in clinic for IUD insertion, if the subject is interested in participating, they will again be counseled about the study and will be given time to ask questions and have their questions answered. If they are eligible to continue, informed consent will be obtained, and they will be randomized to one of the two treatment arms, traditional IUD insertion versus transabdominal ultrasound-guided insertion.

4.3 Recruitment materials

None

4.4 Eligibility/screening of subjects

Not applicable

5.0 Consent Process and Documentation

5.1 Consent Process

5.1.1 Obtaining Informed Consent

5.1.1.1 Timing and Location of Consent

Subjects will be consented at their clinic visit prior to undergoing their IUD insertion. The subject will have been given the consent form at their previous visit or while inpatient to read at home. We will again discuss the study and answer any and all questions the patient may have. At this appointment, the patient will sign the consent form if they agree to continue in the study.

5.1.1.2 Coercion or Undue Influence during Consent

All subjects will be informed at their visit that their participation in the study is entirely voluntary and they will continue to receive routine care whether they consent or decide not to consent to the study.

5.1.2 Waiver or alteration of the informed consent requirement

A waiver of consent is requested to review medical record information to determine preliminary eligibility to participate in the research

5.2 Consent Documentation

5.2.1 Written Documentation of Consent

The consent process will be documented in writing with the long form of consent documentation at the IUD insertion clinic visit:

- The current IRB approved consent form will be obtained.
- We will verify that we are using the most current IRB-approved version of the study specific consent form and that the consent form is in language understandable to the subject.
- A copy of the consent form will be provided to the subject. Whenever possible the consent form will be provided to the subject in advance of the consent discussion.
- .

5.2.2 Waiver of Documentation of Consent (Implied consent, Verbal consent, etc.)

Not applicable

5.3 Consent – Other Considerations

5.3.1 Non-English Speaking Subjects

Not applicable

5.3.2 Cognitively Impaired Adults

5.3.2.1 Capability of Providing Consent

Not applicable

5.3.2.2 Adults Unable To Consent

Not applicable

5.3.2.3 Assent of Adults Unable to Consent

Not applicable

5.3.3 Subjects who are not yet adults (infants, children, teenagers)

5.3.3.1 Parental Permission

Not applicable

5.3.3.2 Assent of subjects who are not yet adults

Not applicable

6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization

6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

Check all that apply:

☐ **Not applicable, no identifiable protected health information (PHI) is accessed, used or disclosed in this study.** *[Mark all parts of sections 6.2 and 6.3 as not applicable]*

☒ **Authorization will be obtained and documented as part of the consent process.** *[If this is the only box checked, mark sections 6.2 and 6.3 as not applicable]*

☒ **Partial waiver is requested for recruitment purposes only (Check this box if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Full waiver is requested for entire research study (e.g., medical record review studies).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Alteration is requested to waive requirement for written documentation of authorization (verbal authorization will be obtained).** *[Complete all parts of sections 6.2 and 6.3]*

6.2 Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

6.2.1 Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual

6.2.1.1 Plan to protect PHI from improper use or disclosure

Information is included in the Research Data Plan Form.

6.2.1.2 Plan to destroy identifiers or a justification for retaining identifiers

Study information will be destroyed after the research has ended and all institutional/regulatory requirements for data retention have been met

6.2.2 Explanation for why the research could not practicably be conducted without access to and use of PHI

Information must be obtained from the subject's electronic medical record during recruitment to determine eligibility and, in some cases, to confirm information discussed with the subject in regards to their medical history.

6.2.3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization

The waiver is requested only for recruitment to determine subject eligibility to ensure that no medical conditions that fall into the exclusion criteria are present and would thus preclude enrollment. This waiver will minimize the enrollment of subjects' who may ultimately fail to meet the study inclusion/exclusion criteria.

6.3 Waiver or alteration of authorization statements of agreement

Protected health information obtained as part of this research will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other permitted uses and disclosures according to federal regulations.

The research team will collect only information essential to the study and in accord with the 'Minimum Necessary' standard (information reasonably necessary to accomplish the objectives of the research) per federal regulations.

Access to the information will be limited, to the greatest extent possible, within the research team. All disclosures or releases of identifiable information granted under this waiver will be accounted for and documented.

7.0 Study Design and Procedures

7.1 Study Design

Prospective, randomized trial.

7.2 Study Procedures

Table of visits:	Visit 1 Routine Visit	Visit 2 IUD Insertion Visit	Visit 3 Routine 4-6 Week String Check and transvaginal US	Visit 4 6 Month Clinic String Check or Phone Contact
Confirm Inclusion/Exclusion Criteria	X[a]	X[a]		
Complete Demographic form		x		
Consent		X[a]		
Randomization		X[a]		
Complete Visual Analogue Score before and after procedure(VAS)		X[a]	X[a]	X[a]
String check			X[c]	X[a]
Transvaginal US			X[b]	X[a]
Transabdominal US		X[a]		
Adverse Events		X[a]	X[a]	X[a]
Likert Scale			X[a]	X[a]

X[a] - indicates research related events
X[b] – indicates both research and standard of care events
X[c] – indicates routine, standard of care

7.2.1 Visit 1-Pre-Insertion Visit:

All interested women undergoing a scheduled IUD insertion will be screened for inclusion/exclusion criteria by the study coordinator or investigator prior to their clinic visit. Those who meet the inclusion/exclusion will be offered information about the study during their clinic visit. The subject will have the study explained to them in detail by the investigator conducting the clinic visit and will be given ample time to have their questions answered. The subject will be given a copy of the consent form to take home and read prior to their IUD insertion visit. The subject will be given information on how to contact the investigator if she has any questions.

7.2.2 Visit 2 (Consent and IUD insertion)

Consent will be obtained from subjects at their IUD insertion visit. The investigator will again review the study with the patient and any questions the patient has about the study will be addressed. After all questions are answered to the patient's satisfaction written consent will be obtained. Demographic information will be collected from each subject.

Subjects will then be randomized to one of two groups:

Group A: traditional blind IUD insertion.
Group B: transabdominal ultrasound guided IUD insertion.

Subjects will be randomized to either US guided or traditional placement of IUD using 1:1 allocation. The randomization scheme for this study will use variable-size, random permuted blocks to ensure that the number of participants in each treatment arm is balanced after each set of *B* randomized participants, where *B* is the block size. After meeting eligibility criteria and being consented for the study, a subject will be ready to be randomized. Team members that have REDCap access will access REDCap to carry out the randomization assignment. If no team member is available with REDCap access the Co-PI (Linda Li) will be contacted and will enter the relevant subject information into REDCap and REDCap will return a randomization assignment. The randomization will then be relayed to the study team member to carry out the assigned randomization. If REDCap is offline and unavailable at the time of randomization, or Linda Li is not able to be contacted, Barb Scheetz at Penn State Hershey Medical Center will have randomization assignments on paper as a backup hardcopy in order to randomize a patient. Subject in both groups will fill out a visual analogue score (VAS) before and after the procedure grading their pain.

Subjects will be instructed to call the investigator if they experience any abnormal uterine bleeding or problems with their IUD.

7.2.3 Visit 3 (4-6 weeks after Visit 2) Subjects will be scheduled to return to REI clinic 4-6 weeks after insertion of the IUD as routine follow-up. Subjects will be asked about any adverse events. Subjects will be asked to complete the Likert scale to indicate their satisfaction level with their IUD and the Visual Analogue Scale to indicate their level of pain. A routine string check in the form of a speculum exam will be performed in addition to a transvaginal ultrasound to confirm positioning of the IUD. If malposition is determined, then routine care will be to remove the IUD. The ultrasound operator will be blinded to the subject's arm in the study

7.2.4 Visit 4 (Clinic visit or phone Visit-6 months after IUD insertion)

At 6 months subjects will be scheduled to return to REI clinic to have an IUD string check and if no strings are visualized then this will be categorized as malposition and the investigator will continue with routine care and work up Subjects who return to clinic for Visit 4 will also have a transvaginal ultrasound performed.

If the subject does not present for a clinic follow up, then she will be contacted by the Study Coordinator or investigator via phone to see if they still have their IUD in place (and when it was removed or lost).

All subjects will be surveyed for pain with the VAS and any adverse events (including abnormal uterine bleeding) will be recorded. All subjects will be asked to categorically rate their satisfaction with the IUD on a Likert Scale.

7.3 Duration of Participation

The total amount of time for participation in the study is 6 months.

8.0 Subject Numbers and Statistical Plan

8.1 Number of Subjects

The sample will consist of 376 women who are undergoing scheduled IUD insertion, thereby 188 women per arm.

8.2 Sample size determination

The sample will consist of 376 women who are undergoing scheduled IUD insertion. We assume a discontinuation rate of 23% at 6 months for the traditional IUD insertion method based on a large study of experienced clinicians inserting IUDs and a large Cochrane review [2, 3]. We project that the ultrasound guided IUD insertion will have half the discontinuation rate, i.e., it will be 11.5% (due to the correct placement of the IUD in the fundus). A sample size of 338 (169 per group) will provide 80% power to detect a difference in the discontinuation proportions at 6 months of 0.23 in the traditional IUD insertion arm and 0.115 in the ultrasound guided arm using a two-sided test having a significance level of 0.05. However, we anticipate 10% subject dropout for this longitudinal study; therefore, we will enroll a total of 376 subjects.

8.3 Statistical methods

The primary analysis will use an intent-to-treat approach to examine differences in the discontinuation rates in the two treatment arms. A modified Poisson regression approach will be used to compare the treatment arms with respect to the primary outcome of IUD discontinuation [4] . An advantage of this method is that it will provide an estimate of the risk ratio and associated 95% confidence interval for this prospective study as well as providing the flexibility to adjust the analysis for potentially confounding factors (e.g., age at IUD insertion). As a secondary analysis, the Kaplan-Meier survival analysis method will be used to assess time from IUD insertion until IUD discontinuation with the comparison between the two treatment arms performed using the log-rank test. For the Kaplan-Meier analysis, the data from a specific subject will be censored at 6 months if the IUD was still in place at 6 months or it will be censored at the time of subject dropout if the subject dropped out of the study prior to 6 months. We plan on performing an interim analysis to assess efficacy of the intervention around the midpoint of the study.

9.0 Confidentiality, Privacy and Data Management

See the Research Data Plan Review Form

10.0 Data and Safety Monitoring Plan

Abdominal ultrasound is minimal risk and it is not plausible that this intervention would worsens outcomes. The only plausible anticipated risks relate to the risks inherent in the insertion of the IUD. Therefore a DSMB is not applicable for this study.

11.0 Risks

The primary risk to the subject is loss of confidentiality of their private medical information.

Risk of Randomization

Ultrasound: ultrasound is a safe procedure that uses low-power sound waves. There are no known risks. Although ultrasound is a valuable tool, it has limitations. Sound doesn't travel well through air or bone, so ultrasound isn't effective at imaging parts of your body that have gas in them or are hidden by bone.
There is a risk of incidental findings while performing the ultrasound, these will be noted in the chart documentation and followed by your physician as needed.
There is no known risk with transabdominal ultrasound.

Standard of Care: Discomforts associated with IUD include: placement discomfort, missed menstrual periods, cysts on the ovary, headache/migraine, acne, depressed mood, heavy or prolonged menstrual bleeding, vaginal discharge, breast tenderness, nausea, nervousness, inflammation of cervix, vulva, or vagina, pelvic pain during period, back pain, weigh increase, decreased sex drive, pain during intercourse, anemia, unusual hair growth or loss, skin irritations, feeling bloated, swelling of hands and feet, and expulsion. Some serious but uncommon side effects of IUD include: pelvic inflammatory disease, sepsis, and perforation in the event IUD becomes attached to or goes through the wall of the uterus, which may require surgery.

12.0 Potential Benefits to Subjects and Others

12.1 Potential Benefits to Subjects

The possible benefit a subject may experience is greater satisfaction and lower IUD discontinuation rates when insertion is performed with the ultrasound guided insertions method compared to the traditional blind insertion.

12.2 Potential Benefits to Others

Other women will benefit from the knowledge gained by this new method of IUD insertion. Ultrasound guided insertion could lead to more accurate placement of the IUD, less pain, and better satisfaction with the procedure.

13.0 Sharing Results with Subjects

Not applicable.

14.0 Subject Stipend (Compensation) and/or Travel Reimbursements

A travel stipend of $25 will be given to subjects at the 6 month follow up visit.

15.0 Economic Burden to Subjects

15.1 Costs

There are no research-related costs to the subjects for their participation in this study except in the following situation:
Subjects who experience signs and symptoms related to their IUD or have a malpositioned IUD at their 4-6 week visit will have standard of care initiated and either the subject or the subject's insurance company will be responsible for the costs associated with that standard of care treatment.

15.2 Compensation for research-related injury

It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Costs for the treatment of research-related injuries will be charged to subjects or their insurance carriers.

16.0 Resources Available

16.1 Facilities and locations

All research recruitment and procedures will take place in the Women's Health clinic at the Hershey Medical Center or one of the Penn State outpatient clinic sites.

16.2 Feasibility of recruiting the required number of subjects

All women undergoing a scheduled IUD insertion will be offered participation in the study when checking in at the Hershey Medical Center or one of the Penn State outpatient clinic sites, which total an average of 750 IUD insertions annually.
In terms of recruitment, this will be a randomized controlled, single center, prospective, clinical trial. We anticipate enrolling 7-8 women per week over a one year enrollment period. A total of 1.5 years will be required to complete the study after start up; 12 month enrollment period, 6 month observation period.

16.3 PI Time devoted to conducting the research

Dr. Estes is extremely committed to her research and she is familiar with research at this location and the local culture. She has been a PI or a co-investigator on greater than 20 IRB approved research protocols. Dr. Estes sees patients 3 days a week with one day of OR time. When not in clinic, time can be devoted to research projects or seeing study patients.

16.4 Availability of medical or psychological resources

Medical resources will already be available since the participants will be having the procedure in clinic under the care of a physician or licensed nurse practitioner.

16.5 Process for informing Study Team

The PI will communicate via email as main method of communication with the study team.

CITI Training
The investigators and all staff involved in the study will have completed their required Collaborative IRB Training Initiative (CITI) in the protection of human research subjects.

Protocol Procedure Training
Study staff delegated to conduct specific study procedures will be trained on these procedures individually or in a group format. Delegation of responsibility will be documented on the Delegation of Responsibility Log and updated as indicated.

The physician investigators are all trained in IUD insertion and routinely perform the IUD insertion procedure.

17.0 Other Approvals

17.1 Other Approvals from External Entities

Not applicable

17.2 Internal PSU Committee Approvals

Check all that apply:

☐ Anatomic Pathology – Hershey only – Research involves the collection of tissues or use of pathologic specimens. Upload a copy of HRP-902 - Human Tissue For Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ Animal Care and Use – All campuses – Human research involves animals and humans or the use of human tissues in animals

☐ Biosafety – All campuses – Research involves biohazardous materials (human biological specimens in a PSU research lab, biological toxins, carcinogens, infectious agents, recombinant viruses or DNA or gene therapy).

☐ Clinical Laboratories – Hershey only – Collection, processing and/or storage of extra tubes of body fluid specimens for research purposes by the Clinical Laboratories; and/or use of body fluids that had been collected for clinical purposes, but are no longer needed for clinical use. Upload a copy of HRP-901 - Human Body Fluids for Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ Clinical Research Center (CRC) Advisory Committee – All campuses – Research involves the use of CRC services in any way.

☐ Conflict of Interest Review – All campuses – Research has one or more of study team members indicated as having a financial interest.

☐ Radiation Safety – Hershey only – Research involves research-related radiation procedures. All research involving radiation procedures (standard of care and/or research-related) must upload a copy of HRP-903 - Radiation Review Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ IND/IDE Audit – All campuses – Research in which the PSU researcher holds the IND or IDE or intends to hold the IND or IDE.

☒ Scientific Review – Hershey only – All investigator-written research studies requiring review by the convened IRB must provide documentation of scientific review with the IRB submission. The scientific review requirement may be fulfilled by one of the following: (1) external peer-review process; (2) department/institute scientific review committee; or (3) scientific review by the Clinical Research Center Advisory committee. NOTE: Review by the Penn State Hershey Cancer Institute Scientific Review Committee is required if the study involves cancer prevention studies or cancer patients, records and/or tissues. For more information about this requirement see the IRB website at: http://www.pennstatehershey.org/web/irb/home/resources/investigator

18.0 Multi-Site Research

Not applicable

19.0 Adverse Event Reporting

19.1 Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB

Research subjects will be questioned about adverse events by the investigators at study visits 2, 3,and 4 or from the patient record if the patient calls or comes to the clinic or emergency room with a possible adverse event.

In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be (1) unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

20.0 Study Monitoring, Auditing and Inspecting

20.1 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the Penn State quality assurance program office(s), IRB, the sponsor, and government regulatory bodies, of all study related documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g., pharmacy, diagnostic laboratory, etc.).

21.0 Future Undetermined Research: Data and Specimen Banking

21.1

Not applicable

22.0 References

[1]Elsedeek, M. S. (2016) Comparison between the traditional non-guided and a novel ultrasound-guided technique for office fitting of intrauterine contraceptive devices. *International Journal of Gynecology & Obstetrics.* 133 (3), 338-41.
[2]Bednarek, P.H. , Creinin, M. D., Reeves, M. F., Cwiak, C., Espey, E., & Jensen, J. T. (2011). Immediate Versus Delayed Intrauterine Device Insertion After Uterine Apiration. *Obstetrical & Gynecological Survey, 66(10).* 624-5.
[3]Tang, J. H., Lopez, L. M., Mody, S., &Grimes, D. A. (2012). Hormonal and intrauterine methods of contraception for women aged 25 years and younger. *Cochrane Database of Systematic Reviews.*
[4] Zou G. A modified Poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004;10(7):702-706.

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Document Description: Study Informed Consent Form version 01Apr2019
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CONSENT FOR RESEARCH
Penn State College of Medicine
The Milton S. Hershey Medical Center

Title of Project: A randomized controlled trial of ultrasound guided IUD insertion

Principal Investigator: Dr. Stephanie Estes

Address:
500 University Drive
Department of OBGYN Division of REI
Hershey, PA 17033

Telephone Numbers: Weekdays: 8:00 a.m. to 5:00 p.m. (717).531.8478. Pager2870
After hours call (717) 531-8521. Ask for the OB/GYN doctor on 24-hour call.

Subject's Printed Name: _____

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

1. Why is this research study being done?

We are asking you to be in this research because you are a woman who has chosen to have an Intrauterine Device (IUD) inserted inside your uterus. It is sometimes called an IUC or intrauterine contraception.

This research is being done to find out if ultrasound guided placement of IUD has benefit in long-term use. Currently there is little to no data on the use of ultrasound guidance for intrauterine device (IUD) placement which is traditionally inserted without visualization of the inside of the uterus, where the IUD is to be located.

Approximately 376 women will take part in this research study at Hershey Medical Center.

2. What will happen in this research study?

Before any study-related procedures are performed you will be asked to read and sign this consent document. Refer to Table 1 (below) for a summary of visits/procedures.

Visit 1-Pre-Insertion Visit:
At the visit where you decide you wish to have an IUD inserted and if the investigator has determined that you are eligible to participate, he/she will discuss this study with you and this

consent form will be reviewed with you. You will be able to take this form home to read. You will be given a contact number to call if you have any questions about the study prior to your IUD insertion visit. If you are interested in participating you will indicate this at your IUD insertion visit at which time you will be able to ask questions and sign the consent form.

Visit 2 (Consent and IUD insertion)
Your doctor will again review the study with you and any questions you have about the study will be addressed. At this time, written consent will be obtained. You will complete a demographic form. You will be randomly assigned (like the flip of a coin) at this visit to one of the following two groups:
Group A: If you are assigned to this group you will have your IUD inserted by the traditional method of blind insertion. You have a 1 out of 2 (50%) chance of receiving traditional blind insertion.
Group B: If you are assigned to this group you will have your IUD inserted along with abdominal ultrasound guidance. You have a 1 out of 2 (50%) chance of receiving ultrasound guidance insertion
You will also be asked to complete a Visual Analog Scale (VAS) in order to rate on a scale of 1-10 with smiley faces your pain before and after the insertion.
You will be instructed to call the investigator at the contact number listed on the first page of this consent form if you experience any bleeding or problems prior to your next visit.

Visit 3 (4-6 weeks after Visit 2)
You will be scheduled for a routine 4-6 week post insertion follow up appointment at 35 Hope Drive clinic where your doctor will perform the routine follow up with string check. Additionally, your doctor will perform a transvaginal ultrasound to look at the positioning of the IUD.
You will be asked about any problems you may have had with your IUD. You will be asked to complete the Likert scale to indicate your satisfaction so far with your IUD as well as the Visual Analogue Scale to indicate your level of pain.
If your IUD is malpositioned (not in the proper position), you will be withdrawn from the study and a routine standard of care work up will be initiated, meaning the IUD will need to be removed. If your IUD is properly positioned you will continue in the study.

Visit 4 (Clinic visit -6 months after IUD insertion)
At 6 months you will be scheduled to return to the 35 Hope Drive clinic to have another IUD string check. If no strings are visualized then this will be categorized as malposition and your doctor will continue with routine care and work up. If you miss the 6 month follow up appointment you will be contacted via phone by one of the investigators to see if you still have the IUD in place (and when it was removed or lost). You will have a transvaginal ultrasound, be surveyed for pain, report any adverse events (including abnormal uterine bleeding), and you will rate your satisfaction with the IUD by completing the Likert scale.

Table of visits:	Visit 1 Routine Visit	Visit 2 IUD Insertion Visit	Visit 3 Routine 4-6 Week String Check and transvaginal US	Visit 4 6 Month Clinic String Check or Phone Contact
Confirm Inclusion/Exclusion Criteria	X[a]	X[a]		
Complete Demographic form		x		
Consent		X[a]		

Randomization		X[a]		
Complete Visual Analogue Score before and after procedure(VAS)		X[a]	X[a]	X[a]
String check			X[c]	X[a]
Transvaginal US			X[b]	X[a]
Transabdominal US		X[a]		
Adverse Events		X[a]	X[a]	X[a]
Likert Scale			X[a]	X[a]

X[a] – indicates research related events
X[b] – indicates research or routine, standard of care events
X[c] – indicates routine, standard of care events

3. What are the risks and possible discomforts from being in this research study?

IUD insertion risks: The risks of IUD insertion are risks that you would have even if you did not take part in this research. Discomforts and side effects may include placement discomfort, missed menstrual periods, cysts on the ovary, headache/migraine, acne, depressed mood, heavy or prolonged menstrual bleeding, vaginal discharge, breast tenderness, nausea, nervousness, inflammation of cervix, vulva, or vagina, pelvic pain during period, back pain, weigh increase, decreased sex drive, pain during intercourse, anemia, unusual hair growth or loss, skin irritations, feeling bloated, swelling of hands and feet, and expulsion.
Some serious but uncommon side effects of IUD include: pelvic inflammatory disease, sepsis, and perforation in the event IUD becomes attached to or goes through the wall of the uterus.

Transvaginal Ultrasound risks: Transvaginal Ultrasounds are a common and usually painless procedure, however, there may be varying degrees of pressure as a wand is inserted and often moved around to allow for proper visualization. There is a risk of incidental findings while performing the ultrasound, these will be noted in the chart documentation and followed by your physician as needed.

Abdominal Ultrasound risks: There is usually no discomfort from a pressure as the transducer is pressed against the area being examined. If scanning is performed over an area of tenderness, you may feel pressure or minor pain from the transducer.

Other risks:

Risk of randomization: You will be assigned to a study group by chance. The study group you are assigned to may prove to be less effective than the other study group.

Risk of loss of confidentiality: There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from occuring. The confidentiality of your electronic data created by you or by the researchers will be maintained to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

If you experience any unusual symptoms as explained by your study doctor, you should contact the investigator at the number listed on the front of the consent form.

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to me?

There is no guarantee that you will benefit from this research. The possible benefits you may experience from this research study if you are assigned to the ultrasound group include a greater satisfaction and lower IUD discontinuation rate. There is no anticipated benefit if you are assigned to the standard care group.

4b. What are the possible benefits to others?

The results of this research may guide the future use of ultrasound for the placement of IUD's.

5. What other options are available instead of being in this research study?

You may choose not to be in this research study. If you choose not to participate in this research, the IUD will be placed in the traditional manner and without ultrasound guidance.

6. How long will I take part in this research study?

If you agree to take part, it will take you about 6 months to complete this research study. During this time you will have 4 visits to clinic.

7. How will you protect my privacy and confidentiality if I decide to take part in this research study?

7a. What happens to the information collected for the research?

Efforts will be made to limit the use and sharing of your personal research information. In our research files at The Milton S. Hershey Medical Center (HMC) and Penn State College of Medicine (PSU) we will include these identifiers: your name, address, phone number, date of birth, medical record number, and a code ID code.

- A list that matches your name with your code number will be kept in a locked file in Dr. Estes' office.
- Your research records will be labeled with your code number and will be kept in a safe area in Dr. Estes' research office.
- A copy of this signed consent form will be included in your HMC medical record. This means that other HMC healthcare providers will know you are in this study.
- Results of some of the research-related tests (including but not limited to ultrasound findings of IUD positioning) will be kept in your HMC medical record.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

7b. How will my identifiable health information be used?

If you give your consent, health information that can be traced to you will be collected for this research study. In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so. We will use and disclose your information only as described in this form and in the HMC Privacy Notice.

The research team may use the following health information:

- Past, present, and future medical records
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

The following people/groups may see, use, and share your identifiable health information:

- HMC/PSU research staff involved in this study
- The HMC/PSU Institutional Review Board (IRB), a group of people who review the research study to protect subjects' rights and welfare
- The HMC/PSU Human Subjects Protection Office
- The HMC/PSU Research Quality Assurance Office
- Non-research staff within HMC/PSU who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- Federal and state agencies (such as the U.S. Food and Drug Administration, the Office for Human Research Protections, the Department of Health and Human Services, the National Institutes of Health, and other U.S. or foreign government bodies that oversee or review research)
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- A group that oversees the data (study information) and safety of this research
- Organizations that provide independent accreditation and oversight of hospitals and research
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)

These groups may also review and/or copy your original PSU/HMC records while looking at the results of the research study. It is possible that some of the other people/groups who receive your health information may not be required by Federal privacy laws to protect your information. We share your information only when we must, and we ask anyone who receives it from us to protect your privacy.

Because research is an ongoing process, your permission for the use, storage and sharing of your health information will continue indefinitely.

Your privacy rights:

- You have the right to refuse to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you will not be able to take part in this research study.
- You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing using the address on the front of this form. Once permission is withdrawn, you cannot continue to take part in the study.
- If you withdraw your permission, we will stop collecting health information about you for this study; we may continue to use and share your health information that we already have if it is

necessary for safety and scientific soundness of the research study; and we will not be able to take back information that has already been used or shared with others.

- You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. However, you may not be allowed to see or copy certain health information that is a part of this research study. This is only for the period of the study. You will be allowed to see that information when the entire research study is complete.

8. What are the costs of taking part in this research study?

8a. What will I have to pay for if I take part in this research study?

For costs of tests and procedures that are only being done for the research study:.

- You and/or your insurance company will not be charged for the cost of any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your condition.
- The research-related tests and procedures that will be provided at no cost to you include:
  - the transabdominal ultrasound which may or may not be performed for guidance and positioning of the IUD at visit 2
  - the visit 3 transvaginal ultrasound will be provided at no cost to you only if you do not exhibit any signs or symptoms from your IUD. If you experience signs or symptoms related to your IUD, or have a malpositioned IUD, routine, standard of care work up will be initiated for which you or your insurance company will be charged.
  - the visit 4 clinic visit and transvaginal ultrasound performed at that visit.

For costs of medical services for care you would receive even if you were not in this research study:

- You and/or your insurance company will be responsible for the cost of routine medications, tests and procedures that you would receive even if you were not in this research.
- You and/or your insurance company will be billed for the costs of these routine tests and procedures in the usual manner.
- You will be responsible for any co-payments, co-insurance and deductibles that are standard for your insurance coverage.
- You will be responsible for any charges not reimbursed by your insurance company.
- Some insurance companies may not pay for routine costs for people taking part in research studies. Before deciding to be in this research you should check with your insurance company to find out what they will pay for.

If you have any questions about costs and insurance, ask the research study doctor or a member of the research team.

8b. What happens if I am injured as a result of taking part in this research study?

It is possible that you could develop complications or injuries as a result of being in this research study. If you experience a side effect or injury and emergency medical treatment is required, seek treatment immediately at any medical facility. If you experience a side effect or injury and you believe that emergency treatment is not necessary, you should contact the principal investigator listed on the first page of this consent form as soon as possible and the principal investigator will arrange for medical treatment.

HMC/PSU compensation for injury

- There are no plans for HMC/PSU to provide financial compensation or free medical treatment for research-related injury.
- If an injury occurs, medical treatment is available at the usual charge.
- Costs will be charged to your insurance carrier or to you.
- Some insurance companies may not cover costs associated with research injuries.
- If these costs are not covered by your insurance, they will be your responsibility.

When you sign this form you are not giving up any legal right to seek compensation for injury.

9. Will I be paid to take part in this research study?

You will receive $25.00 gift card to cover travel expenses for the 6-month follow-up visit.

10. Who is paying for this research study?

The institution and investigators will be receiving a grant from the HMC Department of Obstetrics and Gynecology.

11. What are my rights if I take part in this research study?

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect medical information from your routine medical care. If you agree, this data will be handled the same as research data. If you withdraw completely from the research study, no further information will be collected and your participation will end. You may discontinue taking part at any time without penalty or loss of benefits to which you are otherwise entitled.

Your research doctor may take you out of the research study without your permission.

- Some possible reasons for this are: continuing in the research would be harmful, your IUD needs to be removed, you become pregnant, you did not follow the instructions of the study doctor, or you experience serious side effects.
- Also, the research doctor may end the research study early.
- If your participation ends early, you may be asked to visit the research doctor for a final visit.

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If I have questions or concerns about this research study, whom should I call?

Please call the head of the research study, Dr. Stephanie Estes at 717-531-8478 weekdays 8AM-5PM or the OBGYN doctor on 24-hour call at 717-531-8521 if you:

- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the research protection advocate in the HMC Human Subjects Protection Office (HSPO) at 717-531-5687 if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns or general questions about the research.
- Have questions about your privacy and the use of your personal health information.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

You may visit the Penn State College of Medicine's Clinical Research web site at http://med.psu.edu/clinical-research/faqs for:

- Information about your rights when you are in a research study;
- Information about the Institutional Review Board (IRB), a group of people who review the research to protect your rights; and
- Links to the federal regulations and information about the protection of people who are in research studies. If you do not have access to the internet, copies of these federal regulations are available by calling the HSPO at (717) 531-5687.

A description of this clinical trial 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.

INFORMED CONSENT AND AUTHORIZATION TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative and have answered any questions he/she has about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

Signature of Person Giving Informed Consent and Authorization

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and agree to allow your information to be used and shared as described above.

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name