Safety and efficacy of a suction cervical stabilizer compared to the standard tenaculum for intrauterine procedures in the clinic setting

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Abbreviations

AE	Adverse Event
HIPAA	Health Insurance Portability and Accountability Act
IRB	Institutional Review Board
PI	Principal Investigator
PHI	Personal Health Information
RCT	Randomized Controlled Trial
SAE	Serious Adverse Event
US	United States
IUD	Intrauterine Device
EMB	Endometrial Biopsy
FDA	Food and Drug Administration

1.0 Background & Rationale

When intrauterine procedures are performed, often the cervix needs to be stabilized to facilitate intrauterine entry. The standard approach for cervical stabilization is an invasive, sharp instrument called a tenaculum. This leaves two punctures on the cervix, which can be painful and bleed, which can prolong any intrauterine procedure (IUD insertion, endometrial biopsy, etc). Aspivix ™ has created a **suction-based atraumatic cervical stabilizer** for use with such intrauterine procedures. The First-in-Woman study (RCT with 100 patients) completed in 2 renowned University Hospitals in Switzerland showed positive results (pain reduced by up to 73% and bleeding occurrence reduced by 78%). This new device is **fully FDA approved**.

I've attached the company's data and the clinical brochure showing the device, explaining how it is used, and data on effectiveness. In addition, this is their RCT publication on the journal *Contraception* on this device, showing the data cited above (Attachment #1).
https://www.contraceptionjournal.org/article/S0010-7824(23)00066-5/fulltext

Aspivix ™ launched the AMBASSADOR PROGRAM, a 3–6-month program with free of charge devices for selected hospitals /clinics willing to test extensively Carevix™ in multiple transcervical procedures.

2.0 Objective(s)

2.1 Primary Objective

2.1.1 Primary Objective: to assess patient-reported pain and provider-reported bleeding. Our hypothesis is that patient-reported pain and provider-reported bleeding comparing Carevix™ to tenaculum will be similar in our American population and with all intrauterine procedures as it was in the European study and with only IUD insertions.

2.2 Secondary Objective

2.2.1 Secondary Objective: to assess provider-reported ease of use and provider satisfaction.

3.0 Outcome Measures/Endpoints

3.1 Primary Outcome Measures

3.1.1 Primary outcome measures: To assess patient-reported pain, a questionnaire provided by Aspivix ™ (Attachment #2) will be done after completing the procedure. This takes, on average, 1 minute to complete.

3.2 Secondary Outcome Measures

3.2.1 Secondary outcome measures: To assess provider-reported bleeding, ease of use and provider satisfaction with the device, the provider will complete a questionnaire following the patient's completion of their portion of the questionnaire (Attachment #2). This takes, on average, 2 minutes to complete.

4.0 Eligibility Criteria

4.1 Inclusion Criteria (to be assessed prior to procedure)

- Age 18 years or older
- Speaks and reads in English
- Able to consent on their own
- Will undergo any intrauterine procedure using the Carevix™ (for exposure group) or using Tenaculum (for Control Group)
- Up to 20 providers performing this procedure
- Provider is willing to use Carevix™ for scheduled procedure

4.2 Exclusion Criteria (to be assessed by provider at time of procedure)

- Vaginal bleeding of unknown origin
- Cervix less than 26 mm in diameter
- Nabothian cyst on anterior lip of cervix
- Cervical myomas
- Cervical abnormalities/shape
- Pregnant

4.3 Other Criteria

4.3.1 If the patient does not require ANY cervical stabilization after consent into either study arm, the subject status will be considered **ineligible** and the patient will not be required to complete any surveys.

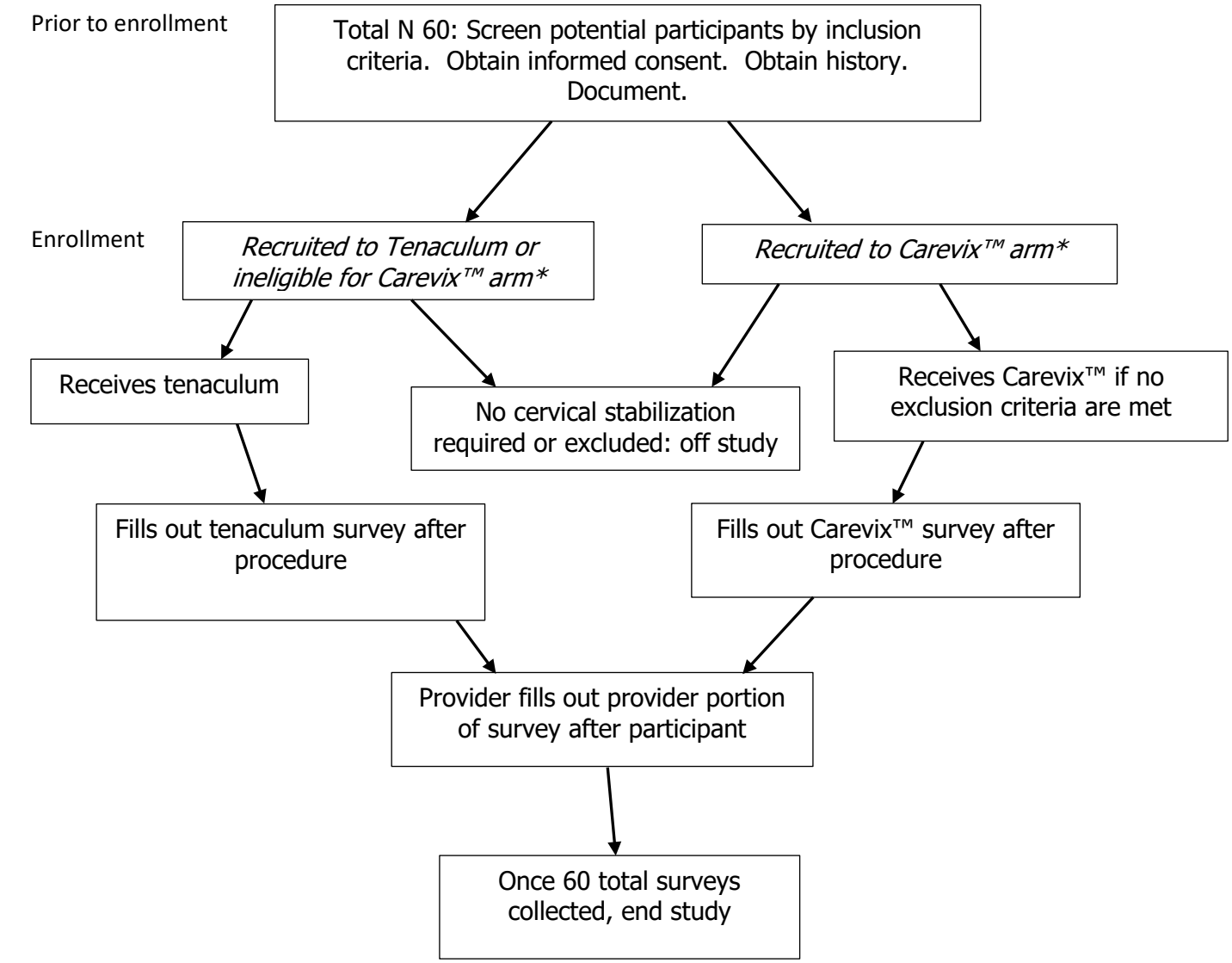
5.0 Study Design

Aspivix, the company that created Carevix™, launched the Ambassador Program, a 3-6 month program with free of charge devices for clinics willing to test Carevix™ in multiple intrauterine procedures. Our clinic, Coleman Center, will conduct a prospective cohort study for 3-6 months where patients who qualify via inclusion criteria who are also receiving an intrauterine procedure (endometrial biopsy, IUD insertion, manual aspiration, etc) on the exposure (Carevix™) arm will have the opportunity to receive the Carevix™ device for cervical stabilization, per provider preference (i.e., providers may decline to use Carevix™ for endometrial biopsy).

Once 25 participants have received Carevix™, recruitment for the control (tenaculum) arm will begin. Participants will receive the standard of care device if cervical stabilization is required. Each participant will be provided with a study information sheet and sign a consent form. They will then undergo their planned procedure, using the assigned device.

Following completion of their procedure, they will also agree to fill out a survey about their experience, which takes about 1 minute to complete. The provider performing the procedure will finish the survey with provider-specific questions about bleeding, ease of use and satisfaction. The purpose of this study is to compare Carevix™ to the tenaculum and determine if the Carevix™ shows similar results in the United States population as it has in the European study and with all intrauterine procedures.

Flow diagram for prospective cohort study



*Once 25 of 30 patients received Carevix™, will commence control group collection
N = 30

6.0 Enrollment

We intend to enroll twenty-five evaluable Carevix subjects prior to commencing the enrollment of the control-group tenaculum subjects. An additional five Carevix subjects (for a total of N=30) will be concurrently enrolled while accruing the thirty additional tenaculum subjects for a total enrollment of N=60.

7.0 Study Procedures

Any intrauterine procedure already scheduled will otherwise proceed accordingly as part of clinical care. During the enrollment, patients who fit above inclusion criteria and are scheduled for an intrauterine procedure may be offered the opportunity to participate in this program and trial the new Carevix™ device during the exposure recruitment period and complete a short survey. If the patient consents to the use of Carevix™ Ambassador program, the suction-based cervical stabilizer will be used on their cervix to stabilize the cervix during the procedure instead of the traditional tenaculum. If the patient or provider opts out of the use of Carevix™, they will be asked if they'd like to participate in the study with the tenaculum. During the tenaculum enrollment phase, patients will receive the standard of care device and complete a short survey.

Following completion of the procedure, the patient will then fill out the patient-based survey. Following the completion of the patient's questions, the provider will then fill out the provider-based survey.

The questionnaire for the Carevix™ Ambassador program will be stored within the Aspivix company database (all questions are HIPAA compliant and do not reveal PHI). The survey is labeled as originating from Indiana University for easy access to only our patient data.

8.0 Study Calendar

There is no study calendar – the patient will have their intrauterine procedure scheduled and will decide if they wish to participate in the Carevix™ Ambassador program or not. The event will be a one-time procedure only when the Carevix™ suction-based cervical stabilizer is used or the tenaculum is used.

9.0 Reportable Events

It is not anticipated that there will be Serious Adverse Effects as defined by the FDA (death, life-threatening complications, need for hospitalization, disability or permanent damage, or an intervention needed to prevent permanent impairment or damage). However, if one occurs, it will be promptly reported to the IU IRB and sponsor (within 5 days of knowing about the occurrence) and per IU HRPP policy if unexpected, related/possibly related to participation and if the SAE suggests that the research places the subject or others at greater risk of harm.

Other adverse events (AE) that may occur with any cervical stabilization device, such as bleeding or injury at stabilization site needing medication or surgical intervention, are common and will be collected and reported as part of study data and at annual regulatory reviews.

10.0 Data Safety Monitoring

This study is no greater than minimal risk. Data safety and monitoring will be performed by the database manager for the Qualtrics database and the PI. Data quality, subject recruitment data completion, outcome and adverse event data, and proper consent procedures will be regularly reviewed by the PI, study coordinator, and data manager at least monthly. A formal Data Safety Monitoring Board is not required. While no formal stopping criteria are proposed, monitoring of AEs will be ongoing and will be discussed by the PI and Department representatives if the AE rate (notably bleeding or injury to the stabilization site on the cervix) is above 50%.

11.0 Study Withdrawal/Discontinuation

Patients can decline participation and will receive standard of care if cervical stabilization is required. Patients who consent to receiving the Carevix™ and who require no cervical stabilization or is assessed by the provider to be otherwise ineligible for the device will be considered ineligible if they do not receive tenaculum (unless consented for tenaculum) and will not be required to complete any surveys or follow-ups.

12.0 Statistical Considerations

We performed sample size/power calculations with the primary outcome of pain (visual analog scale) at the time of Carevix™/tenaculum use. Thirty participants per group (total N=60) are needed to achieve at least 80% power and a two-sided 5% significance level. Descriptive characteristics of those in the Carevix™ and control groups will be compared using standard statistical testing such as Chi-square and t-tests. Differences in outcomes between the device and control groups will similarly utilize standard testing.

13.0 Statistical Data Management

Primary data for the exposure group (e.g. the Carevix™ group) will be collected via Aspivix's secure server. Aspivix has agreed in the Ambassador Agreement to allow access to their data. In the provider section of the survey will be a link to select location site and these data will be separately accessible. The surveys for the patient and provider are connected within the same survey. The data for the control group (e.g. the tenaculum group) will be collected and stored via RedCap, using similar questions to the exposure survey. Aspivix will also furnish us with raw data that will allow us to correlate the date and time of the submitted survey with the date and time of the patient's consented information. This data will be documented in RedCap for the purpose of data analysis. The signed consent forms will be stored in a secure and lockable cabinet.

14.0 Privacy/Confidentiality Issues

None of the questions on the data collection questionnaire will contain PHI. Data will be stored within the company Aspivix's secure server and on RedCap.

15.0 Follow-up and Record Retention

The study will last about 1 year (6 months for Carevix™ exposure group and approximately 6 months for the control group (e.g. tenaculum). The record retention will be indefinite.

16.0 References

Yaron M, et al. Safety and efficacy of a suction cervical stabilizer for intrauterine contraceptive device insertion: Results from a randomized, controlled study. *Contraception*. Vol 123, July 2023. https://www.contraceptionjournal.org/article/S0010-7824(23)00066-5/fulltext

17.0 Appendix

Attachment #1: Carevix™ data published in the journal *Contraception*.
Attachment #2: Questionnaire for patients and providers (done through the same link).
Attachment #3: Study information sheet and consent form.