Research Plan

Proposal Title	A prospective, multicenter, randomized controlled clinical trial protocol to evaluate the safety and efficacy of uterine stents in preventing intrauterine adhesions.
Version number	Version 2.1
Revision Date	2020-11-28
Contract Research Organization	Hunan Haokang Medical Technology Co., Ltd.
principal investigators	Professor Xue Min
Main research units	Xiangya Third Hospital of Central South University
Clinical trial type	Medical device clinical trials
Indications	Used for the prevention and treatment of intrauterine adhesions.
Experimental Objective	Evaluate the efficacy of uterine stents in preventing intrauterine adhesions after intrauterine procedures and whether their safety meets clinical requirements.
Experimental Design	This trial employed a prospective, multicenter, randomized, controlled, non-inferiority clinical trial design. The target population consisted of 200 women aged 20-40 years with intrauterine adhesions and surgical indications (those desiring fertility or experiencing obstructed menstrual flow). These women were randomly assigned to either the experimental or control group, with 100 patients in each group. The experimental group underwent hysteroscopic adhesiolysis followed by intrauterine stent placement , while the control group received intrauterine IUDs,

	balloons, and sodium hyaluronate gel placement. Both groups underwent three artificial cycles post-operatively, followed by a follow-up hysteroscopy during hospitalization.
Sample size	200 cases This trial was a 1:1 randomized, parallel-controlled, non-inferiority clinical trial . A reduction of one or more levels in the AFS score was used as the primary efficacy endpoint. Based on prior research data and clinical significance of the investigational product, the sample size was estimated using the internationally recognized sample size estimation software PASS11.0, resulting in a total sample size of at least 168 cases. Considering the possibility of dropouts or loss to follow-up during the trial , and also for ease of case allocation, the number of cases was increased to 100 cases per group, for a total of 200 cases across both groups.
Number of research centers	3
Case selection criteria	Selection criteria: ① Patients clinically diagnosed with intrauterine adhesions and who have surgical indications (referring to those who wish to have children or have obstructed menstrual flow). ②Women aged 20-40; ③ Participants voluntarily participate in the trial, and each participant signs an informed consent form. Exclusion criteria: ① Patients with significantly abnormal uterine cavity shape after surgery ; patients whose normal uterine cavity anatomical morphology cannot be clearly separated (i.e., the openings of both or one fallopian tubes are not visible); patients with reproductive organ malformations;

	patients with excessively large or small uterine cavities; patients with recent uterine perforation; and patients with cervical insufficiency. ②Those with a history of intrauterine adhesions and who have received treatment; ③Those with endometrial tuberculosis or suspected endometrial tuberculosis; ④ Those with adenomyosis or uterine fibroids > 4cm; ⑤ Those with a history of malignant tumors or suspected of having malignant tumors; ⑥ Patients with concurrent acute or chronic intrauterine infections and genital infections; ⑦ Unexplained vaginal bleeding or suspected malignant uterine lesions; ⑧Those with severe anemia and coagulation disorders; those with a history of thrombosis; ⑨ Individuals in the acute phase of various diseases or those with severe systemic diseases; ⑩ Individuals with severe mental illness or those who are too weak to tolerate this surgery; ⑪ Individuals with severe heart, liver, or kidney dysfunction; ⑫ Those with contraindications to anesthesia or surgery; ⑬ Those who have participated in clinical trials in the past three months. ⑭ Those whom the researchers deemed unsuitable for inclusion.
Research suspension criteria	① If a participant is unwilling or unable to continue the clinical trial, they may request to withdraw from the trial. ②If a serious safety issue occurs during the test, the test should be stopped immediately.

	③ If the product is found to have no clinical value during the trial, the trial should be terminated. ④ If a major error is found in the clinical trial protocol during the trial, making it difficult to evaluate the product effect; or if a serious deviation occurs in the implementation of the clinical trial protocol, making it difficult to evaluate the product if the trial continues, the trial should be terminated. ⑤ The applicant requests termination (e.g., due to funding or management reasons). ⑥ The State Food and Drug Administration ordered the suspension of the trial for some reason.
Research Instruments	Uterine stents will be used in the trial.
Research Reference Instruments	A uterine ring, a size 12 Foley catheter, and sodium hyaluronate gel will be used in the trial.
Instructions for use of research equipment	This instrument should be used in accordance with this experimental protocol and the manufacturer's instructions, and is for single use only. ① Tear open the packaging bag and take the product out of the packaging bag, taking care to prevent the product from being contaminated; ② Before placement, the depth of the uterine cavity should be measured first, and the position of the positioning block should be adjusted so that the distance between the top of the uterine support and the positioning block is equal to the measured depth of the uterine cavity; ③ Dilate the cervix at least 7-8 times (depending on the tightness of the cervix), and fix the uterine stent to the top of the placement tube; ④ Insert the uterine stent together with the placement device into the

	uterine cavity, fix the push rod, withdraw the placement tube about 1cm, gently push the placement tube towards the fundus of the uterus once, and push the uterine stent to the fundus of the uterus. Then withdraw the push rod together with the placement tube out of the uterine cavity. ⑤ After placement, check whether the product position and size are appropriate. If necessary, replace with a uterine stent of appropriate size or adjust the position under endoscopy. ⑥ Regular ultrasound monitoring after placement (the specific monitoring time is determined by the clinician based on the severity of the condition) to check whether the uterine stent is in place. ⑦ The clinician will determine the timing of removal based on the patient's condition. Removal requires dilation to 8mm and forceps removal under direct hysteroscopic visualization. Removal is recommended after treatment is completed.
The study referenced the instrument's instruction manual.	This instrument should be used in accordance with this experimental protocol and the manufacturer's instructions, and is for single use only. ① Open the packaging bag and take the uterine ring out of the packaging bag, taking care to prevent the product from being contaminated; before insertion, the depth of the uterine cavity should be measured first, and the uterine ring should be inserted into the uterine cavity after dilation; after insertion, check whether the position and size of the uterine ring are appropriate, and replace it with an appropriate size uterine ring or adjust its position under a microscope if necessary ; ②Take the No. 12 Foley catheter out of the packaging bag, cut off the tip with scissors, clamp the tip of the catheter with curved forceps and insert it into the uterine cavity. Use a syringe to draw 2.5ml of normal saline and inject it into the catheter balloon. Inject 2ml of hyaluronic acid gel into the uterine cavity through the other catheter.

	③ Tie a knot at the lower end of the No. 12 Foley catheter, wrap the tail end with sterile gauze, and secure it to the patient's groin with adhesive tape. After 24 hours, cut the catheter with scissors, completely release the saline solution from the balloon, and slowly pull the balloon out.
Combination therapy	Artificial cycle regimen (not applicable if there are contraindications to estrogen and progesterone therapy): For the first artificial cycle, begin oral estradiol valerate on the day of the procedure, at a dose of 3 mg twice daily, until day 25 of the menstrual cycle. For the last 6 days, add progesterone capsules 200 mg daily, taken before bedtime. For the second and third artificial cycles, begin oral estradiol valerate on day 5 of the menstrual cycle, at a dose of 3 mg twice daily, for 21 consecutive days. For the last 6 days, add progesterone capsules 200 mg daily.
Study endpoints	**Key indicators:** AFS score: A reduction of ≥ 4 points in the total AFS score for adhesions is considered effective. The effectiveness rate is calculated as: (Number of cases with a reduction of ≥ 4 points in the total AFS score / Total number of cases) × 100%. Efficacy assessment: Markedly effective: IUA grade decreases by 1-2 levels, and no obvious adhesions are seen in the uterine cavity; Effective: IUA grade decreases by 1-2 levels, but adhesions remain in the uterine cavity; Ineffective: IUA grade remains the same as before the procedure or worsens. **Secondary indicators:** ①Menstrual recovery rate: Record changes in menstrual flow before and after surgery, and compare the improvement in menstruation between the experimental group and the control group. ② Quality of life assessment scale, assessed before device placement and 1, 3 and 4 months after placement.

	③ Ease of product implementation for researchers: Does the outer packaging meet the requirements? Is it easy to remove the packaging? Is it easy to place the product into the designated area of the uterus?
Statistical considerations	Statistical analysis plan: The statistical analysis plan is developed by biostatistics experts and principal researchers based on the research protocol, and data verification and finalization are completed and documented. The statistical analysis software used is SAS version 9.4. General principles: Select appropriate statistical descriptive and inference methods based on the experimental design type, data type, and data distribution characteristics. All statistical tests are two-tailed tests, and a p-value less than or equal to 0.05 is considered statistically significant. For quantitative data, the statistical description should include the mean, standard deviation, median, minimum, and maximum values; for qualitative data, the frequency and percentage of each level should be given . This clinical trial uses a single-sample target value method. The primary effect indicator, image sharpness, is qualitative data. A 95% confidence interval for overall image sharpness is calculated. If the lower limit of this interval is greater than the set value of 90%, the experimental device is considered necessary for clinical application.

Head record

I. Applicant Information

(I) Name of the applicant: Hunan Haokang Medical Technology Co., Ltd.

(II) Applicant's Address: 3rd Floor, Yannong Building, Intersection of Luquan Road and Lusong Road , High-tech Development Zone, Changsha City, Hunan Province

(III) Applicant's contact information: 18874147387 Contact person: Zheng You

(iv) Relevant qualification documents of the applicant

Corporate Business License Number: 4301930000260471.5

Medical Device Production License No.: 湘食药监械生产许 20150066 号

II. List of all clinical trial institutions and investigators in multicenter clinical trials

Organization Code	Clinical trial institution name	Researchers	job title	Contact information
01	Xiangya Third Hospital of Central South University	Xue Min	professor	13687354678
02	Beijing Tiantan Hospital	Feng Limin	Chief Physician	
03	Changsha No.1 Hospital	Yang Jing	Chief Physician	13637406291

III. Objectives and Contents of Clinical Trials

(a) Purpose

the effectiveness of uterine stents in preventing intrauterine adhesions

after intrauterine procedures and whether they meet the safety criteria for clinical use.

(II) Content

This trial employed a prospective, multicenter, randomized, controlled, non-inferiority clinical trial design. The target population consisted of 200 women aged 20-40 years with intrauterine adhesions and surgical indications (those desiring fertility or experiencing obstructed menstrual flow). These women were randomly assigned to either the experimental or control group, with 100 patients in each group. The experimental group underwent hysteroscopic adhesiolysis followed by intrauterine stent placement , while the control group received intrauterine IUDs, balloons, and sodium hyaluronate gel placement. Both groups underwent three artificial cycles post-operatively, followed by a follow-up hysteroscopy during hospitalization.

IV. Background information on clinical trials

Intrauterine adhesions (IUA), also known as Asherman's syndrome, refers to a pathological phenomenon where the uterine cavity and/ or cervical canal partially or completely close due to damage to the basal layer of the endometrium caused by various factors (uterine procedures, infection, postpartum abortion curettage, uterine malformations, interventional therapy, radiation, etc.). Its incidence is on the rise in China. Intrauterine adhesions may be asymptomatic or manifest as decreased menstrual flow, amenorrhea,

periodic lower abdominal pain, infertility, and obstetric complications such as recurrent miscarriage and placental abnormalities. Due to the high recurrence rate after intrauterine adhesion surgery, treatment outcomes are poor, and there is currently no unified treatment plan or definitive treatment method. Statistics show that the re-adhesion rate after transcervical resection of adhesion (TCRA) is as high as 62.5%, and the pregnancy success rate is only 22.5%-33.3%, seriously affecting women's reproductive health. Clinical medical staff are constantly exploring and seeking the best treatment methods to improve the final pregnancy rate and pregnancy outcome, and reduce the burden on patients and society.

The 2015 Chinese expert consensus on the clinical diagnosis and treatment of intrauterine adhesions pointed out that: (1) IUA patients without clinical symptoms and without fertility requirements do not need surgical treatment. (2) Patients with oligomenorrhea but without fertility requirements and without dysmenorrhea or hematometra do not need surgical treatment. (3) For patients with infertility, recurrent miscarriage, oligomenorrhea and fertility requirements, TCRA can be used as the first-line treatment. The purpose of IUA treatment is to restore the anatomical shape and volume of the uterine cavity, treat related symptoms (infertility, pain, etc.), prevent the formation of re-adhesion, promote endometrial regeneration and repair, and restore fertility. On the other hand, the treatment

of endometrial regeneration difficulties has little effect, and we face a huge challenge in the treatment of intrauterine adhesions. Regarding the management of IUA surgery, that is, measures to prevent re-adhesion after IUA surgery, the expert consensus proposes intrauterine devices (IUDs), intrauterine support balloons, biological adhesive materials, etc. In addition, estrogen can promote endometrial growth and regeneration, which helps wound repair. Currently, the intrauterine device used clinically to prevent re-adhesion of the surgical site after TCRA is mainly the IUD. Its main component is a copper-containing stainless steel ring. The purpose is to use the metal support of the IUD to prevent the surgically separated adhesions from coming into contact again and forming new adhesions. However, the effectiveness of IUD placement is not ideal because the effective area of its metal support is limited to the perimeter, and it cannot completely separate the anterior and posterior walls of the uterine cavity. This allows for re-adhesion of the uterine cavity walls outside the IUD, and may even cause the IUD to be partially embedded in the adhered tissue, leading to IUD entrapment. Furthermore, the released copper ions can cause a sterile inflammatory reaction, which is detrimental to the treatment of intrauterine adhesions . Other intrauterine devices, such as the COOK balloon and Foley catheter, also have their own limitations and are not suitable for long-term intrauterine placement. These devices can compress the endometrium,

causing ischemia and further damage, and the catheter's indwelling in the vagina can cause discomfort and reduce the patient's quality of life. Hyaluronic acid gel, injected into the uterine cavity via a catheter, covers the uterine wall and exerts a certain anti-adhesion effect. However, the adhesion time is only 48-72 hours, limiting its use to the early postoperative period. In summary, there is currently no highly effective, safe, and simple material or method for preventing recurrence of intrauterine adhesions after surgery. Developing an innovative technology that overcomes the shortcomings of the aforementioned methods—an ideal, dedicated anti-adhesion device for intrauterine adhesions—is expected to be the key technological bottleneck in this field.

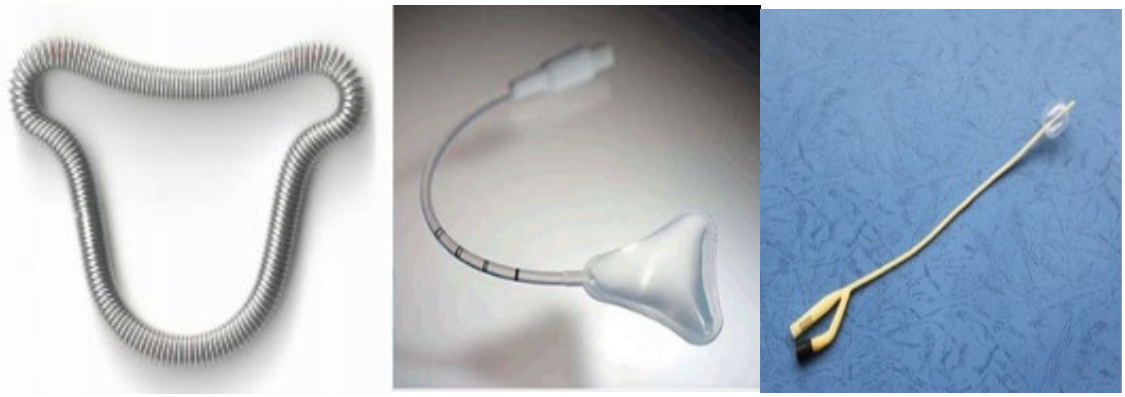


Figure 1. Uterine ring; Figure 2. COOK balloon stent; Figure 3. Foley catheter.

Considering the shortcomings of current intrauterine devices for preventing intrauterine adhesions and the actual conditions of clinical application, Hunan Haokang Medical Technology Co., Ltd. has developed a

uterine-shaped silicone treatment device—a uterine stent—that can effectively prevent recurrence of intrauterine adhesions after separation surgery. It is made of medical-grade silicone rubber, which is non-irritating, non-toxic, non-carcinogenic, has good biocompatibility, is corrosion-resistant, and will not swell, soften, or deteriorate due to water absorption. It is easy to process and manufacture, convenient to use, and has good thermal stability. In vivo biocompatibility and in vitro cytotoxicity studies of this new material have been completed, and animal experiments on the uterine stent have yielded satisfactory results. It is believed that this uterine stent will effectively prevent recurrence of intrauterine adhesions after surgery. Following discussions at a researcher meeting, this clinical trial protocol was formulated.

In summary, considering the causes and characteristics of intrauterine adhesions, their occurrence is widespread, not limited by region or population, and is a nationwide or even international disease. Hysteroscopic adhesiolysis under direct visualization remains the gold standard for its surgical treatment, with no significant differences in surgical procedures. There is no unified standard for postoperative intrauterine adhesiolysis methods; therefore, a multicenter randomized controlled trial is needed to evaluate the effectiveness and safety of uterine stent placement in preventing intrauterine adhesions.

V. Product characteristics, structural composition, working principle, mechanism of action, and testing range

(I) Product Features

This product mainly consists of a reinforcing ring, a membrane, a tail-shaped structure, and a placement device. The placement device consists of a placement sleeve, a positioning block, and a push rod. The reinforcing ring is elastic, and its shape and size are adapted to the periphery of the uterine wall. The membrane is connected inside the reinforcing ring. The product is characterized by its tail-shaped structure, which is connected to the midpoint of the lower section of the reinforcing ring and is longitudinally solid. The lower section of the reinforcing ring also has three drainage grooves, which facilitate the drainage of uterine cavity fluid, prevent infection caused by poor drainage, and promote endometrial growth (see Figures 1 and 2).

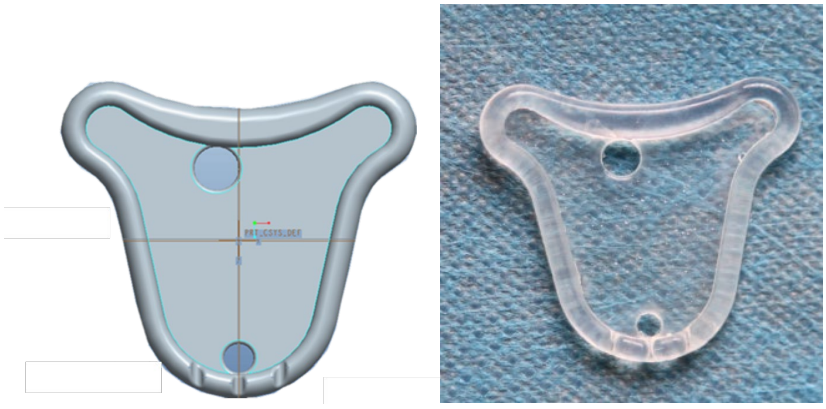


Figure 4 Schematic diagram of uterine stent; Figure 5 Sample image of uterine stent.

(II) Product structure, working principle, and mechanism of action

1. Product Structure Composition

This uterine stent is made of medical-grade silicone rubber, a material

that has been widely used in clinical practice. Its safety and reliability have been proven. It is non-irritating to human tissues, has no toxic side effects, is non-carcinogenic, has good biocompatibility, is corrosion-resistant, and will not swell, soften, or deteriorate due to water absorption. It is easy to process and manufacture, convenient to use, and has good thermal stability.

2. Working principle

This product is made of medical-grade silicone rubber and mainly consists of a uterine-shaped reinforcing rib , a membrane, a tail-shaped structure, and a placement device composed of a placement sleeve, a positioning block, and a push tube . The uterine-shaped reinforcing rib is elastic, and its shape and size are adapted to the periphery of the uterine wall. Three drainage grooves are provided at the lower end of the uterine-shaped reinforcing rib, which is more conducive to the drainage of uterine cavity fluid and reduces the chance of intrauterine infection due to poor drainage. The membrane completely separates the contact between the anterior and posterior walls of the uterine cavity, physically preventing adhesions between them. Furthermore, because the membrane is very thin, it exerts almost no pressure on the endometrium it contacts. The tail-shaped structure is mainly used to prevent adhesion recurrence. This longitudinal, solid tail-shaped structure connects to the midpoint of the lower segment of the uterine-shaped ring and communicates with the uterine cavity. Its length can be

trimmed according to the patient's specific situation, effectively preventing adhesions in the lower segment of the uterine cavity and the internal cervical os, while maximizing material savings, reducing manufacturing costs, and providing better drainage of uterine cavity fluid.

3. Working principle

Intrauterine adhesions mainly result from damage to the endometrium, leading to the formation of fibrotic adhesions on the anterior, posterior, and lateral walls of the uterine cavity. This product is made of medical-grade silicone rubber, with a thin silicone membrane in the middle. This thin silicone membrane does not compress the endometrium, preventing secondary damage such as ischemia. Simultaneously, it acts as a physical barrier after intrauterine adhesion separation surgery, blocking adhesions on the anterior, posterior, and lateral walls of the uterine cavity and preventing recurrence after intrauterine procedures or adhesion separation surgery. The tail structure of the device can block adhesions at the lower end of the uterine cavity, preventing recurrence of adhesions at the lower end of the uterine cavity or the internal cervical os. Two round holes on the membrane facilitate the placement and removal of the device, while three small grooves at the lower end facilitate the drainage of intrauterine fluid and menstrual blood, preventing and reducing the occurrence of intrauterine infection.

(III) Scope of the Test

The subjects of this clinical trial were women who had undergone intrauterine procedures for the treatment of intrauterine adhesions .

VI. Indications, contraindications, and precautions for the product

(a) Indications

Used for the prevention and treatment of intrauterine adhesions.

(ii) Contraindications

① This procedure is contraindicated in patients whose uterine cavity shape is significantly abnormal after intrauterine procedures .

② Contraindicated in patients with concurrent acute or chronic intrauterine infections;

③ Patients with recent uterine perforation, excessively small or large uterine cavity, cervical insufficiency, or unexplained vaginal bleeding;

④ Those suspected of having malignant endometrial lesions;

⑤ Use with caution in other situations deemed inappropriate by clinicians.

(III) Precautions

①This product should be placed by professional medical personnel, and strict aseptic operation should be performed during the placement process.

②This product has been sterilized with ethylene oxide and should be

used immediately after opening the packaging bag;

③This product and its container are single-use sterile products and must not be reused. They should be disposed of after use.

④ Please check the packaging before use. Do not use if the product has expired or the packaging is damaged.

⑤ After placement, it is necessary to check whether the uterine stent is placed correctly. If it is not placed correctly, it should be adjusted accordingly or removed immediately.

⑥ This product is contraindicated for individuals with silicone allergies.

⑦ Uterine stents are not designed for contraception; use condoms for contraception during use.

VII. Overall Design

(a) Experimental Design

1. Experimental Objective

To evaluate the efficacy of uterine stents produced by Hunan Haokang Medical Technology Co., Ltd. in preventing intrauterine adhesions after intrauterine procedures and whether they meet the safety requirements for clinical use.

2. Selection of experimental methods and the rationale

This clinical study adopted a multicenter, open-label, parallel randomized controlled non-inferiority clinical trial design because the

appearance of the devices varies greatly, making it inconvenient to set up a blinding method.

Control Group Selection: Both the 2015 Chinese Expert Consensus on the Clinical Diagnosis and Treatment of Intrauterine Adhesions (IUA) and the 2017 American Association of Gynecological Laparoscopists (AAGL) guidelines on IUA mention postoperative management, specifically measures to prevent re-adhesion after TCRA, including methods such as IUDs, Cook balloons, Foley catheters, and hyaluronic acid gel. Currently, there is no unified standard for adjuvant treatments after TCRA. Considering that the expanded balloon after the Cook balloon stent is opened may compress the endometrium, causing ischemic damage, hindering patient movement, and causing significant discomfort, the Cook balloon was not selected as a control group in this clinical trial. However, the combination of an IUD + balloon + sodium hyaluronate gel is currently a well-established clinical practice, and therefore this method was chosen as the control group.

3. Measures to reduce or avoid bias

Researcher training: Before the start of a clinical trial, the monitor, together with the heads of each trial center, should train the researchers on the trial protocol so that the researchers can understand and become familiar with the trial process. At the same time, they should also be aware of all new information related to the product that is discovered during the clinical trial

to ensure that the researchers implement the trial protocol.

Clinical trial monitoring: Monitors appointed by the sponsor conduct regular on-site monitoring visits to the trial hospitals to ensure strict adherence to all aspects of the study protocol and to verify the original data against the information on the case report forms.

4. Investigational medical devices and control medical devices/control diagnostic and treatment methods

The experimental group received a uterine stent. After TCRA, different sizes of uterine stents were inserted into the uterine cavity according to the different uterine cavity morphologies of the subjects. The position of the uterine stents was adjusted by hysteroscopy again. The control group received a uterine IUD + balloon + sodium hyaluronate gel. Subjects underwent TCRA surgery in the hospital. After the surgery, different sizes of uterine IUDs were selected and inserted into the uterine cavity according to the uterine cavity morphology. At the same time, a 12-gauge Foley catheter was left in the uterine cavity. 2.5 ml of normal saline was injected into the balloon of the catheter, and 2 ml of hyaluronic acid gel was injected into the uterine cavity through one side of the catheter. The Foley catheter was removed by the doctor on the first day after the surgery. Both the experimental and control groups received 3 artificial cycles after the surgery and were hospitalized for follow-up hysteroscopy.

Note: ① Artificial cycle regimen (not applicable if there are contraindications to estrogen and progesterone therapy): For the first artificial cycle, start taking estradiol valerate orally on the day of the procedure, at a dose of 3 mg twice daily, until day 25 of the menstrual cycle. For the last 6 days, add progesterone capsules 200 mg daily, taken before bedtime. For the second and third artificial cycles, start taking estradiol valerate orally on day 5 of the menstrual cycle, at a dose of 3 mg twice daily, for 21 consecutive days. For the last 6 days, add progesterone capsules 200 mg daily, taken before bedtime.

②The hospitalization time for surgery is 2-7 days after menstruation ends or within the 8th-14th day of the menstrual cycle.

5. Preservation of instruments

(1) The experimental instruments shall be uniformly labeled and numbered, and marked as being for clinical research use only. There shall be a designated person to check and record the process.

(2) The test equipment shall be delivered directly to each research center by a designated person of the applicant, and the research center and the applicant shall establish a complete handover procedure for the test equipment.

(3) Each research unit shall establish a designated location for storing experimental equipment. The storage location shall be a dry, well-ventilated

indoor environment free from corrosive gases.

(4) Each research unit shall establish a strict management system for experimental devices. These devices shall be managed by designated personnel other than the research physicians, and a dedicated "Clinical Trial Medical Device Usage Record Form" shall be established. After the trial, the experimental devices shall be returned to the sponsor in a centralized manner.

All experimental instruments shall be uniformly labeled and numbered, and marked with the words "For clinical research use only". The label template is as follows (actual labels will be attached separately):

Test equipment Number: XXX (For clinical research use only) Provided by Hunan Haokang Medical Technology Co., Ltd.

6. Random grouping

To avoid potential bias in participant selection and randomization due to the predictability of treatment regimens, the trial employed a center-stratified block randomization method. Randomization coding was generated on a computer by statisticians using the PLAN procedure in SAS software (setting factors such as seed number, sample size, number of blocks, and stratification). The randomization scheme was concealed using sequentially

coded, opaque, sealed envelopes.

7. Subject selection (including, if necessary, selection of a control group)

(1) Selection criteria

① Patients clinically diagnosed with intrauterine adhesions and who have surgical indications (referring to those who wish to have children or have obstructed menstrual flow).

②Women aged 20-40;

③ Participants voluntarily participate in the trial, and each participant signs an informed consent form.

Note: All of the above conditions must be met for a candidate to be selected.

(2) Exclusion criteria

① Patients with significantly abnormal uterine cavity shape after surgery ; patients whose normal uterine cavity anatomical morphology cannot be clearly separated (i.e., the openings of both or one fallopian tubes are not visible); patients with reproductive organ malformations; patients with excessively large or small uterine cavities; patients with recent uterine perforation; and patients with cervical insufficiency.

②Those with a history of intrauterine adhesions and who have received treatment;

③Those with endometrial tuberculosis or suspected endometrial

tuberculosis;

④ Those with adenomyosis or uterine fibroids > 4cm;

⑤ Those with a history of malignant tumors or suspected of having malignant tumors;

⑥ Patients with concurrent acute or chronic intrauterine infections and genital infections;

⑦ Unexplained vaginal bleeding or suspected malignant uterine lesions;

⑧Those with severe anemia and coagulation disorders; those with a history of thrombosis;

⑨ Individuals in the acute phase of various diseases or those with severe systemic diseases;

⑩ Individuals with severe mental illness or those who are too weak to tolerate this surgery;

⑪ Individuals with severe heart, liver, or kidney dysfunction;

⑫ Those with contraindications to anesthesia or surgery;

⑬ Those who have participated in clinical trials in the past three months.

⑭ Those whom the researchers deemed unsuitable for inclusion.

(3) Criteria and procedures for stopping trial/trial treatment

The criteria for terminating a trial are as follows: the clinical trial is

terminated before it has been completed according to the protocol. The purpose of terminating the trial is primarily to protect the rights of the participants, ensure the quality of the trial, and avoid unnecessary economic losses.

① If a participant is unwilling or unable to continue the clinical trial, they may request to withdraw from the trial.

②If a serious safety issue occurs during the test, the test should be stopped immediately.

③ If the product is found to have no clinical value during the trial, the trial should be stopped.

④ If a major error is found in the clinical trial protocol during the trial, making it difficult to evaluate the product effect; or if a serious deviation occurs in the implementation of the clinical trial protocol, making it difficult to evaluate the product if the trial continues, the trial should be stopped.

⑤ The applicant requests termination (e.g., due to funding or management reasons).

⑥ The State Food and Drug Administration ordered the cessation of the trial for some reason.

Procedure for stopping the experiment:

①When a subject requests to withdraw from the trial, the researcher should communicate with the subject as much as possible, ask for the reasons,

record the condition of the equipment, and complete the assessment items that can be completed.

② If a trial must be stopped due to safety concerns, researchers should take appropriate treatment measures to actively rescue the subjects based on their actual condition . They should also record the last time the experimental product was used and complete all available assessment items.

③ For all cases where the trial was stopped, a trial summary form and the reason for stopping the trial should be filled in on the case report form.

(4) Planned enrollment time

The earliest enrollment date for the first subject is expected to be December 2017, and the latest enrollment date for the last subject is expected to be August 2018.

(5) The expected overall duration of the clinical trial and the rationale for determining it.

Expected duration: 14 months. This includes time for protocol development and ethics considerations (3 months), enrollment and data collection (9 months), data analysis and report writing (2 months).

(6) Expected duration of participation for each participant

The entire process for each participant, from informed consent and assessment to surgery and three post-operative hysteroscopic follow-up examinations, is expected to last approximately three months.

(7) Number of subjects required for clinical trials

This trial was a 1:1 randomized, parallel-controlled, non-inferiority clinical trial . A reduction of one or more levels in the AFS score was used as the primary efficacy endpoint. Based on prior research data and clinical significance of the investigational product, the sample size was estimated using the internationally recognized sample size estimation software PASS11.0, resulting in a total sample size of at least 168 cases. Considering the possibility of dropouts or loss to follow-up during the trial , and also for ease of case allocation, the number of cases was increased to 100 cases per group, for a total of 200 cases across both groups.

8. Validity Evaluation Methods

(1) Explanation of validity parameters

The AFS scores before and after hysteroscopic separation were used to assess the intrauterine adhesion rate in the experimental and control groups (referencing the 2017 American Fertility Association (IUA) guidelines).

AFS scoring sheet for the extent of intrauterine adhesions, pathological types of adhesions, and changes in the patient's menstrual cycle.

Extent of intrauterine adhesion lesions		
Score	evaluate	This is a description
1		cumulative area of adhesions is less than 1/3 of the total area of the uterine cavity .
2		accumulated area of adhesions is less than 1/3 to 2/3 of the total area of the uterine

		cavity .
4		cumulative area of adhesions is less than 2/3 of the total area of the uterine cavity.
Adhesive properties		
Classification	evaluate	This is a description
1		Membranous adhesions
2		fibrous adhesions
4		Dense muscular adhesions
Improved menstruation		
Classification	evaluate	This is a description
0		Normal menstrual flow
2		Decreased menstrual flow
4		amenorrhea
Total score		
Score	**evaluate**	**Adhesion evaluation**
1-4 (Mild)		Mild adhesion
5-8 (Moderate)		Moderate adhesions
9-12 (Severe)		Severe adhesions

(2) Selection of methods and timing for evaluating, recording and analyzing validity parameters

Key indicators:

AFS score: A reduction of ≥ 4 points in the total AFS score for adhesions is considered effective. The effectiveness rate is calculated as: (Number of cases with a reduction of ≥ 4 points in the total AFS score / Total

number of cases) × 100%.

Significant effect: IUA grade decreased by 1-2 levels, and no obvious adhesions were observed in the uterine cavity.

Effective treatment: IUA grade decreased by 1-2 levels, but intrauterine adhesions remained.

Ineffective: IUA grade is no different from or worsens compared to preoperative level.

Secondary indicators: ① Menstrual recovery rate: Record changes in menstrual flow before and after surgery, and compare the improvement in menstruation between the experimental group and the control group.

② Quality of life assessment scale, assessed before device placement and 1, 3 and 4 months after placement (see Appendix 1).

③ Ease of product implementation for researchers: Does the outer packaging meet the requirements? Is it easy to remove the packaging? Is it easy to place the product into the designated area of the uterus? (See Appendix 2)

9. Safety evaluation methods

(1) Explanation of safety parameters

① Vital signs (body temperature, respiration, heart rate, blood pressure).

②Laboratory tests:

Routine vaginal discharge test (cleanliness, fungi, trichomonas, BV)

Urine HCG test

Complete blood count (white blood cell count, red blood cell count, hemoglobin count, platelet count, platelet count)

Liver and kidney function (alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, blood urea nitrogen, creatinine)

Electrolytes (sodium, potassium, magnesium, calcium)

Coagulation function (prothrombin time PT, activated partial thromboplastin time APTT)

③ 12-lead electrocardiogram

④ Gynecological examination (vulva, vagina, cervix, uterus, and bilateral adnexa).

⑤ Adverse events: Abdominal pain, lower abdominal discomfort, abnormal vaginal bleeding, abnormal vaginal discharge may occur; whether adverse events such as entrapment, breakage, detachment, displacement, ectopic placement, deformation, and intrauterine infection occur during the 3-month period after the device is placed in the subject's uterine cavity.

(2) Selection of methods and timing for evaluating, recording and analyzing safety parameters

10. Screening Indicators

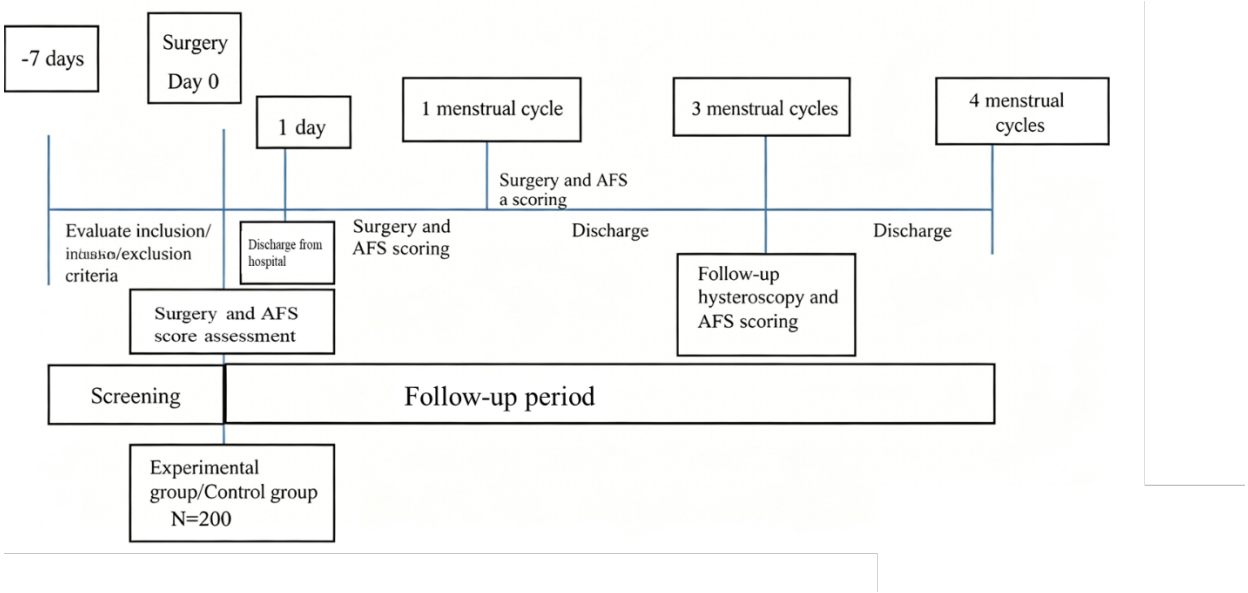
Chest X-ray, gynecological vaginal ultrasound, and pre-transfusion examinations (hepatitis B, hepatitis C, syphilis, HIV) were recorded once

before enrollment.

Note: If a patient has undergone chest X-ray, gynecological vaginal ultrasound, or pre-transfusion examination within one month prior to enrollment and can provide the examination report or a copy thereof, then the examination does not need to be repeated.

(II) Test Procedure

1. Experimental Flowchart



project	Visit					
	Screening period (-7 to 0 days)	Surgery (0 days)	Post-surgery (1 day)	Days 8-14 after one menstrual cycle following the procedure (20 ± 10 days).	Days 8-14 after 3 menstrual cycles following the surgery (80 days ± 20 days)	Postoperative period: 8-14 days after 4 menstrual cycles (100 days ± 30 days)

	V1	V2	V3	V4	V5	V6
Sign Informed Consent Form	X					
Demographic data	X					
Taking medical history	X					
marital and reproductive history	X					
Menstrual history						
History of intrauterine adhesions	X					
Accompanying diseases and treatment history	X					
vital signs	X	X	x		x	
Gynecological examination	X			x		x
AFS score		X			x	
Selection and exclusion criteria		X				
Random grouping		X				
Laboratory tests						
routine vaginal discharge	X			x	x	x
Blood routine	X				x	
Liver and kidney	X				x	

function						
Coagulation function	X				x	
electrolytes	X				x	
Pre-transfusion examination #	X					
Chest X-ray #	X					
electrocardiogram	X				x	
Gynecological vaginal ultrasound examination #	X					
Combined medication						
Artificial cycle medication		x	x	x	x	
Other combined medications						
Evaluate						
AFS score		X			x	
Changes in menstrual flow				x	x	x
Quality of life assessment				x	x	x
Ease of implementation for researchers		X			x	
Adverse events		X	x	x	x	x
Serious adverse events		x	x	x	x	x

End of experiment						

Note: ① x represents mandatory items. If additional laboratory tests are required, please record them as well.

② # indicates that if this examination was performed one month prior to enrollment and the results or a copy can be provided, the examination does not need to be repeated.

2. Visit Plan

(1) Visit 1, screening period (-7~0 days)

①Informed consent

② The following preoperative data must be collected within 7 days before the surgery: Demographic data of the subject (birth date, ethnicity), vital signs examination (body temperature, pulse, respiration, heart rate, blood pressure), gynecological examination (examination of vulva, vagina, cervix, uterus, and bilateral adnexa), and medical history (past medical history of this disease, history of other diseases, and marital and reproductive history).

③ Laboratory tests

routine vaginal discharge

Urine HCG test

Complete blood count, liver and kidney function tests

electrolytes

Coagulation function

12-lead electrocardiogram

In addition, chest X-rays, gynecological vaginal ultrasound examinations, and pre-transfusion examinations are valid if performed within one month prior to

enrollment.

④ Combined medication use

(2) Visit 2, surgery (0 days)

① Vital signs detection;

②Surgery : AFS score;

③ Verify the inclusion/exclusion criteria;

④ Random grouping;

⑤ Recording of adverse events;

⑥ Combined medication use.

(3) Visit 3, post-surgery (1 day):

① Vital signs detection;

② Adverse event records;

③ Combined medication use;

④ Remove Foley balloon No. 12 from the control group.

(4) Visit 4: 8-14 days after the first menstrual cycle following the operation (20 days ± 10 days)

① Gynecological examination;

②Routine vaginal discharge test;

③ Adverse events;

④ Inquire about the medication used in the artificial cycle;

⑤ Quality of life assessment;

⑥ Combined medication use;

(5) Visit 5: 8-14 days after the 3-month postoperative menstrual cycle (80 days ± 20 days)

① Vital signs;

② Gynecological examination;

③Routine vaginal discharge test, urine HCG test, complete blood count, liver and kidney function tests, coagulation function tests, and electrolyte tests;

④ Electrocardiogram (ECG);

⑤ Inquire about the medication used during the artificial cycle.

⑥ Quality of life assessment

⑥ Surgery: AFS score;

⑦ Adverse events;

⑧ Combined medication use.

9. Inquire whether there have been any changes in menstrual flow.

⑩ Researcher Product Implementation Ease of Use Assessment

(6) Visit 6: 8-14 days after the 4th menstrual cycle following the operation (100 days ± 20 days)

① Gynecological examination;

②Routine vaginal discharge test;

③ Adverse events;

④ Combined medication use.

⑤ Quality of life assessment

⑥ Inquire whether there have been any changes in menstrual flow.

3. Medical Device Usage Standards

Uterine stent group usage guidelines :

① Tear open the packaging bag and take the product out of the packaging bag, taking care to prevent the product from being contaminated;

② Before placement, the depth of the uterine cavity should be measured first, and the position of the positioning block should be adjusted so that the distance between the top of the uterine support and the positioning block is equal to the measured depth of the uterine cavity;

③ Dilate the cervix at least 7-8 times (depending on the tightness of the cervix), and fix the uterine stent to the top of the placement tube;

④ Insert the uterine stent together with the placement device into the uterine cavity, fix the push rod, withdraw the placement tube about 1cm, gently push the placement tube towards the fundus of the uterus once, and push the uterine stent to the fundus of the uterus. Then withdraw the push rod together with the placement tube out of the uterine cavity.

⑤ After placement, check whether the product position and size are appropriate. If necessary, replace with a uterine stent of appropriate size or adjust the position under endoscopy.

⑥ Regular ultrasound monitoring after placement (the specific

monitoring time is determined by the clinician based on the severity of the condition) to check whether the uterine stent is in place.

⑦ The clinician will determine the timing of removal based on the patient's condition. Removal requires dilation to 8mm and forceps removal under direct hysteroscopic visualization. Removal is recommended after treatment is completed.

Control group: IUD + Foley catheter + hyaluronic acid gel usage guidelines :

① Open the packaging bag and take the IUD out of the packaging bag, taking care to prevent the product from being contaminated; before insertion, the depth of the uterine cavity should be measured first, and the IUD should be inserted into the uterine cavity after dilation; after insertion, check whether the position and size of the IUD are appropriate, and replace it with an appropriate size IUD or adjust its position under a microscope if necessary ;

② Remove the No. 12 Foley catheter, cut off the tip with scissors, clamp the tip of the catheter with curved forceps and insert it into the uterine cavity. Draw 2.5ml of normal saline into the catheter balloon with a syringe, and inject 2ml of hyaluronic acid gel into the uterine cavity through the other catheter.

③ Tie a knot at the lower end of the No. 12 Foley catheter, wrap the tail

end with sterile gauze, and secure it to the patient's groin with adhesive tape. After 24 hours, cut the catheter with scissors, completely release the saline solution from the balloon, and slowly pull the balloon out.

(III) Monitoring Plan

1. The sponsor has commissioned a third-party monitoring agency to monitor this clinical trial.

2. Monitors should have relevant professional backgrounds in clinical medicine, pharmacy, biomedical engineering, statistics, etc., and have undergone necessary training. They should be familiar with the management standards and relevant regulations for clinical trials of medical devices, as well as non-clinical and clinical information of similar products of investigational medical devices, and clinical trial protocols and related documents.

3. Each center should be monitored at least once every 2-4 weeks, and the frequency of monitoring should be increased appropriately depending on the enrollment situation.

4. Monitors should follow the GCP principle and supervise the conduct of clinical trials to ensure that they are strictly implemented according to the protocol. Trial data should be true, complete and accurate. Specific responsibilities include: (1) confirming before the trial that the clinical trial institution has the appropriate conditions, including staffing and training, complete laboratory equipment, good working conditions, an estimated

number of subjects, and that the researchers involved are familiar with the trial requirements; (2) monitoring the clinical trial institution and researchers before, during and after the trial to see if they comply with the approved clinical trial protocol, medical device clinical trial management regulations or relevant laws; (3) confirming that each subject has signed an informed consent form before participating in the trial, and understanding the subject enrollment rate and the progress of the trial. Follow-up that the researchers failed to do, trials that were not conducted, examinations that were not performed, and whether errors or omissions were corrected should be clearly and truthfully recorded. For revised informed consent forms, confirm that subjects whose visits have not ended have signed again; (4) confirming that all case report forms are filled out correctly and are consistent with the original data. All errors or omissions have been corrected or noted, and have been signed and dated by the researchers. (5) Confirm and record the types of diseases, total number of cases, gender, age, and treatment effects of the cases; (6) Confirm and record the situations in which subjects withdraw from the study or fail to comply with the requirements of the informed consent form, and discuss such situations with the investigator; (7) Confirm that all adverse events and device defects have been recorded, and report and record serious adverse events and major device defects that may lead to serious adverse events within the prescribed time; (8) Be responsible for monitoring the supply, storage, use, maintenance and post-

trial processing of medical device samples for the investigation; (9) Ensure that the investigator receives the latest version of all documents related to the clinical trial; (10) After each monitoring, a written report shall be submitted to the sponsor, which shall state the monitoring date, time, monitor's name, monitoring location, investigator's name, inspection content, project completion status, monitoring findings, facts, deviations, conclusions and corrections to errors and omissions.

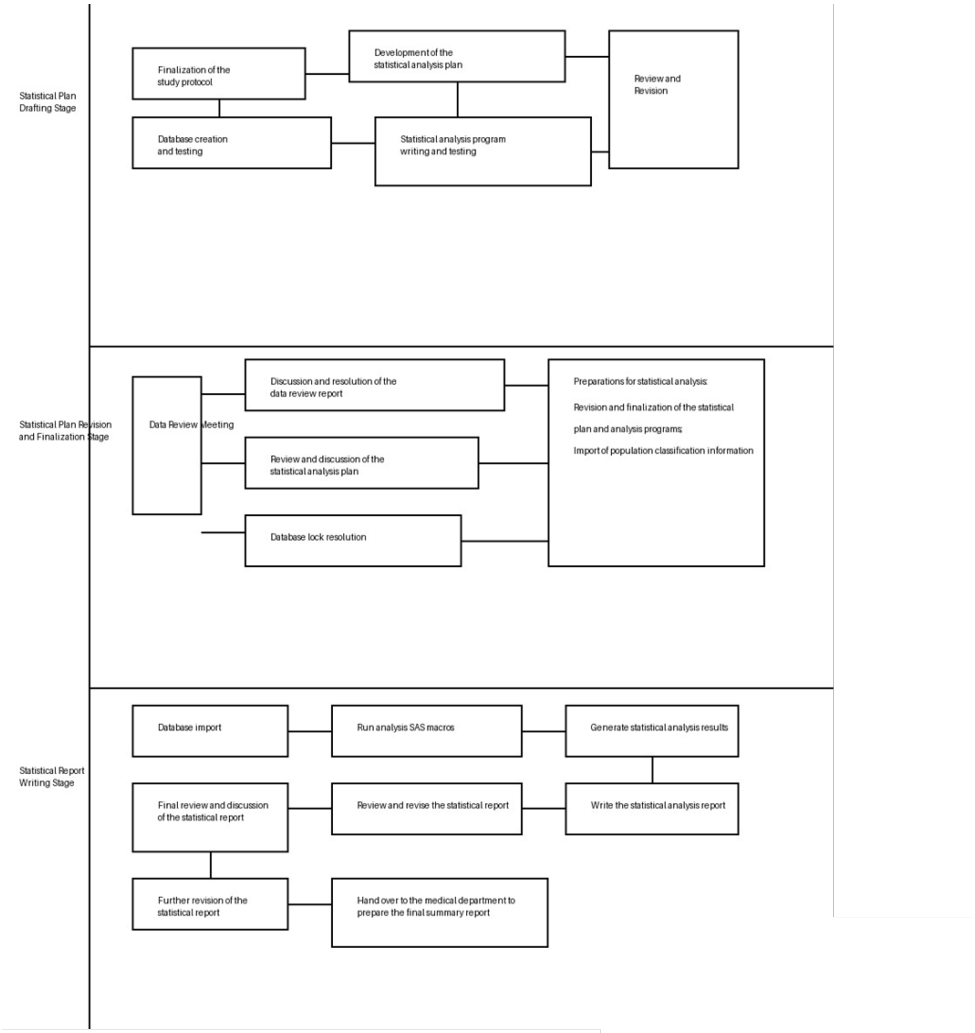
VIII. Statistical Considerations

(I) Statistical Design, Methods and Analytical Procedures

1. Statistical Design

This study aimed to evaluate the efficacy and safety of uterine stents in preventing recurrence of adhesions after hysteroscopic adhesiolysis. It employed a multicenter, randomized, controlled, open-label, non-inferiority clinical trial design. Due to the unique nature of medical devices, their appearance cannot be standardized; therefore, this trial was designed as an open-label trial.

2. Statistical Analysis Procedures



(ii) Calculation of sample size

1. Calculation of sample size

The value was set to 1.645 after setting α=0.025 (one-sided), the non-inferiority margin was δ=10%, and the beta (80% power) was β=0.84. The case ratio of the experimental group to the control group was r=1:1. According to the treatment methods and treatment effectiveness statistics of intrauterine adhesions used in the Department of Obstetrics and Gynecology of Xiangya

Third Hospital, the effective rate of intrauterine adhesions in the control group within 1 month after surgery was n=92.65%. The sample size (experimental group + control group) was calculated using the statistical formula $M=2*2*n*(1-n)*((\alpha+\beta)/\delta)^2$

The sample size was 168 cases.

This study was a multicenter, parallel, controlled, non-inferiority design clinical trial. The primary effect endpoint was the intrauterine adhesion rate after adhesiolysis. The sample size was calculated using the following formula:

$$N=\left[\frac{Z_{\alpha}\sqrt{P_0(1-P_0)}+Z_{\beta}\sqrt{P_0(1-P_0)}}{P-P_0}\right]^2$$

2. Number of clinical trials for each disease and the rationale for determining this number.

Taking into account the shedding factor (the shedding rate is about 15 %), the final sample size was increased to 200 cases, including 100 cases in the experimental group and 100 cases in the control group.

Note: 92.65% effective rate for intrauterine adhesions: Considering that there is currently no unified method for treating intrauterine adhesions, multiple methods are needed to prevent recurrence. The Chinese expert consensus on the clinical diagnosis and treatment of intrauterine adhesions and the intrauterine adhesions guidelines jointly developed by the American

Association of Endoscopy (AAGL) and the European Society for Endoscopy and Gynecology (ESGE) both mention methods such as anti-adhesion barriers (IUD, stents, catheters, etc.), hyaluronic acid gel, and artificial cycles. The current treatment regimen of IUD + balloon + sodium hyaluronate gel has not been reported in the literature in terms of the effectiveness of AFS score. Therefore, the IUD + balloon + sodium hyaluronate gel regimen was selected from patients with intrauterine adhesions admitted to Xiangya Third Hospital of Central South University in 2016. The clinical evaluation showed an effective rate of 92.65%.

3. In multicenter clinical trials, the minimum and maximum number of participants at each clinical trial site and the rationale.

Three centers participated in this trial, with each hospital planning to allocate a minimum of 40 subjects and a maximum of 120 subjects.

(iii) Significance level and power of clinical trials

1. Difference test

Using $\alpha=0.05$ as the significance level, a two-tailed test is employed. The statistical method, statistic, and specific P-value are provided. A P-value less than or equal to 0.05 is considered statistically significant.

2. Non-inferiority test

Based on the power of 80% ($\beta=0.2$) used in the sample estimation, with $\alpha=0.025$ as the test level, a one-sided 95% confidence interval is used for the

test. If the lower limit of the 95% confidence interval of the difference in efficacy is greater than the given non- inferiority threshold (δ=-10%), then the experimental group can be considered non-inferior to the control group.

(iv) Expected shedding rate

It is expected that during the trial, the percentage of subjects who fail to withdraw or are lost to follow- up for various reasons will not exceed 15%.

(v) Criteria for acceptance/disacceptance of clinical trial results

Calculation of the primary efficacy endpoint: During statistical analysis, the difference in efficacy rates and its 95% confidence interval will be calculated. If the lower limit of the 95% confidence interval for the difference in efficacy rates between the experimental and control groups is greater than the given non- inferiority margin (δ=-10%), then the experimental group can be considered non-inferior to the control group, meaning the experimental product has met the trial objective (qualified) requirements. Conversely, if the lower limit is greater than the lower limit, then the experimental group cannot be considered non-inferior to the control group, meaning that based on the current clinical trial data and sample size, the experimental product cannot be considered to have met the trial objective (qualified) requirements.

(vi) Criteria and reasons for terminating the trial based on statistical reasons

This clinical trial does not plan to conduct an interim analysis; therefore, it should not be terminated without specific reasons . The clinical trial will be

terminated if the investigators believe that the clinical application effect of the tested medical device is unsatisfactory or may cause significant harm to the subjects.

(vii) The statistical methods used for all data, including the handling of missing, unused, or erroneous data (including those dropped out or withdrawn midway) and unreasonable data.

Before conducting formal data analysis, missing and outlier values should be checked. If a particular indicator has a large number of missing values , sensitivity analysis should be performed; missing values that cannot be filled should be discarded during statistical analysis. When an indicator value deviates from the upper or lower quartile by more than twice the interquartile range, that value is considered an outlier. When analyzing indicators with outliers, outlier removal analysis and outlier retention analysis should be performed. If the results of the two analyses are inconsistent, conclusions should be drawn with caution.

Based on the experimental design type, data type, and data distribution characteristics, select appropriate statistical descriptive and inference methods. For quantitative data, the statistical description should include the mean, standard deviation, median, minimum, and maximum values; for qualitative data, the frequency and percentage of each level should be given . This clinical trial uses a single-sample target value method. The primary effect

indicator, image sharpness, is qualitative data. Calculate the 95% confidence interval for overall image sharpness. If the lower limit of this interval is greater than the set value of 90%, the experimental device is considered necessary for clinical application.

(viii) Procedures for reporting deviations from the original statistical plan

When the statistical methods in the original statistical plan cannot meet or are unsuitable for the statistical analysis of actual clinical trial data, and the statistical analysis plan needs to be modified (e.g., added, deleted, or changed in parts or methods), it must be discussed and signed off by the researchers, statisticians, sponsors, and other relevant personnel. The original statistical analysis plan will remain unchanged; the corresponding modifications will exist as supplementary documents to the original plan and will be submitted for review.

(ix) Selection criteria and rationale for including subjects in the analysis

The statistical analysis dataset for this experiment was determined to be the following three datasets:

① The full analysis set (FAS) refers to an ideal population of subjects that closely approximates the ITT (Independent Testing Tolerance) principle. It should include data from all subjects.

② Per Protocol Set (PPS): This is a subset of the full analysis set where each participant demonstrates good compliance and does not violate

the protocol. Generally, it refers to cases in the full analysis set that meet the following three criteria: a. Complete primary endpoint values; b. Meeting inclusion, exclusion, and cut-off criteria; c. Fully compliant with the protocol.

③ The Safety Set (SS) should include all enrolled cases who underwent at least one examination and at least one safety assessment.

IX. Data Management

Define experimental data: All data generated in this experiment shall be saved as experimental data, including raw data and secondary data generated from the raw data.

Case Report Form (CRF) Completion and Transfer: Researchers must promptly, completely, accurately, and clearly input data into the CRF based on the subjects' original observation records. Each enrolled case must complete a CRF. Monitors will ensure the trial is conducted according to the protocol, confirming that all CRFs are completed correctly and completely, and consistent with the original data. Any errors or omissions will be promptly addressed by requesting corrections from the researcher. Corrections must maintain the original records' legibility and must be signed and dated by the researcher. After review by the clinical monitor, the first copy of the completed CRF is transferred to the data administrator for data entry and management.

Data entry and modification: Data entry and management are the responsibility of the data administrator designated by the statistical unit. To ensure the accuracy of the data, two data administrators should independently perform double entry and verification, and set up logical check items in the database. The data administrators verify the data in the case report forms. If any questions are found, they are asked to the researchers through the clinical monitor in the form of a question form. The data administrators modify and confirm the data based on the researchers' answers. If necessary, the question form can be issued again. The software used for data entry is DBASE. After the data entry and inspection are completed, the data is reviewed and the final definition and judgment of the analysis population are completed. The data can be locked when the following conditions are met: (1) All data has been entered into the database; (2) All questions have been resolved.

10. Feasibility Analysis

(a) Analysis of the probability of success

This experimental product is an independently developed product. The safety performance of the medical-grade silicone rubber used in this product meets national safety standards, therefore its expected safety performance is reliable. Its technical performance indicators meet the registration product standards and are expected to meet the requirements of clinical trials, with a high likelihood of patient acceptance. Its design aims to prevent intrauterine

adhesions through physical barriers, which is theoretically feasible. The trial organizers and implementers are all professionals familiar with clinical validation, and the trial was strictly conducted in accordance with the "Good Clinical Practice for Medical Devices" issued by the State Food and Drug Administration, laying a solid foundation for the trial's success in terms of product quality and technology.

(II) Analysis of the probability of failure

(1) The reasons for the failure of the trial may be: patients are unwilling to accept the use of the new product; improper case selection; improper clinical operation; and the product is not placed in the uterine cavity for a long time and does not meet the design requirements.

(2) Corresponding measures: Strengthen communication with subjects to obtain their full understanding and cooperation, and obtain informed consent before the trial; select experienced clinicians with intermediate or senior professional titles to perform the procedures; strictly screen subjects according to the inclusion criteria of the trial protocol; if any abnormalities such as functions or results that do not meet expectations occur during the clinical trial, the relevant personnel of the sponsor and the research unit shall jointly analyze and study the situation to determine the cause of the abnormality, whether it is a product problem or improper clinical use, and implement solutions after specific analysis to ensure the continuation of the clinical trial. If the clinical

trial fails due to product defects, the clinical trial shall be stopped immediately, and the sponsor shall further improve the product. If the improved product does not meet the registration standards, the standards shall be revised and the registration test shall be carried out again according to the new standards. The clinical validation shall be carried out again after passing the new standards.

XI. Quality Control of Clinical Trials

(1) Researcher training: Before the start of a clinical trial, the person in charge of the trial unit should train the researchers on the trial protocol.

(2) Measures to improve subject compliance: Researchers should strictly implement informed consent to ensure that subjects fully understand the trial requirements and cooperate with the trial.

(3) Monitoring of clinical trials: Monitors appointed by the sponsor will conduct regular on-site monitoring visits to the trial hospitals to ensure that all contents of the study protocol are strictly followed and to check the original data to ensure that they are consistent with the contents of the case report forms.

12. Ethical Issues and Informed Consent in Clinical Trials

(a) Ethical considerations

Clinical trials must be conducted in accordance with the Declaration of Helsinki and relevant Chinese regulations and guidelines for clinical trial research. Before a trial can begin, the ethics committee of the institution responsible for the clinical trial must approve the trial protocol.

Before each participant is enrolled in this study, the research physician is responsible for providing them or their designated representative with a complete and comprehensive written explanation of the study's purpose, procedures, and potential risks. Participants should be informed that they have the right to withdraw from the study at any time. A written informed consent form must be provided to each participant before enrollment, and the research physician is responsible for ensuring that each participant obtains informed consent before entering the study. This informed consent form should be retained as part of the clinical trial documentation for future reference.

(ii) Approval of the test plan

Uterine stents are classified as Class III medical devices and are not included in the "Catalogue of Class III Medical Devices Requiring Clinical Trial Approval". Therefore, they do not require approval from the State Food and Drug Administration before conducting clinical trials.

(III) Informed consent process and informed consent form text

The researchers will provide participants with a detailed explanation of the background, purpose, procedures, benefits, and risks of the trial, and answer any questions they may have. Participants will fully understand the background, purpose, procedures, risks, and benefits of the trial, and after receiving answers to their questions, they will sign an informed consent form voluntarily participating in the study. (Informed consent form attached as

Appendix 3).

XIII. Regulations for Reporting Adverse Events and Device Defects

(a) Adverse events

Adverse events (AEs) are adverse medical events that occur during clinical trials, regardless of whether they are related to the investigational medical device.

(ii) Serious adverse events

Serious Adverse Event (SAE): refers to an event that occurs during a clinical trial that results in death or a serious deterioration of health condition, including fatal illness or injury, permanent defects in body structure or function, hospitalization or prolonged hospitalization, or the need for medical or surgical intervention to avoid permanent defects in body structure or function.

(iii) Reporting procedures and contact information

All adverse events and device defects discovered during clinical trials must be recorded by the investigators, who shall jointly analyze the causes with the sponsor, prepare a written analysis report, and propose opinions on continuing, suspending, or terminating the trial. This report shall be submitted to the ethics committee for review by the medical device clinical trial management department of the clinical trial institution. In the event of a serious adverse event, the investigator shall immediately take appropriate

treatment measures for the subject and simultaneously report in writing to the medical device clinical trial management department of the affiliated clinical trial institution, which shall then notify the sponsor in writing. The medical device clinical trial management department shall, within 24 hours, report in writing to the relevant ethics committee and the provincial, autonomous region, or municipal food and drug administration department and health and family planning authority where the clinical trial institution is located. For deaths, the clinical trial institution and investigators shall provide all necessary information to the ethics committee and the sponsor. For serious adverse events and device defects that may lead to serious adverse events, the sponsor shall, within 5 working days of learning of the event, report to the food and drug administration department and the corresponding health and family planning authority, and simultaneously notify other participating clinical trial institutions and investigators, whose medical device clinical trial management departments shall promptly notify the ethics committee of that clinical trial institution.

(iv) Contact person and contact information of the leading unit and the applicant

unit	Contact Person	Contact number	fax	address
applicant	Hunan Haokang	18874147387	0731-85839895	3rd Floor, Yannong

	Medical Technology Co., Ltd. Zheng You			Building, Yuelu District, Changsha City, Hunan Province
Central Ethics	Ethics Committee of Xiangya Third Hospital, Central South University Wang Xiaomin	0731-88618938	0731-88618938	No. 138, Tongzipo Road, Yuelu District, Changsha City, Hunan Province
CFDA Registration Division, Research and Supervision Department		010-68313344	010-68586295	Building 2, No. 26 Xuanwumen West Street, Xicheng District, Beijing
National Health and Family Planning Commission		010-68792201		No. 38, Beilishi Road, Xicheng District, Beijing

XIV. Regulations on Deviation from and Amendment of Clinical Trial Protocols

Definition of deviation range:

(1) Subjects who did not meet the inclusion criteria were included in the trial;

(2) The subjects did not sign an informed consent form;

(3) The subjects signed the informed consent form only after participating in the trial;

(4) The subject did not receive treatment as prescribed in the protocol;

(5) Serious adverse reactions were not reported or were not communicated in a timely manner;

(6) The subject used a prohibited drug;

Post-procedure handling of clinical trial protocol deviations: Any deviation from the clinical trial protocol that affects the rights, safety, and health of participants should be promptly reported to the ethics committee by completing a protocol deviation report form. To protect the rights, safety, and health of participants, in emergency situations, deviations from the clinical trial protocol may be made without the prior consent and approval of the sponsor and the ethics committee. Such deviations should be documented and reported to the sponsor and the ethics committee as soon as possible. If the deviation is due to the inability to include a sufficient number of participants using current inclusion and exclusion criteria, the protocol should be revised and reported to the ethics committee for approval and filing.

Regulations on revising clinical trial protocols: If, during the course of

a clinical trial, the investigator believes that the clinical trial protocol has defects (such as inclusion and exclusion criteria not covering the target study population or difficulty in enrolling cases, or insufficient sample size due to the selected parameter values in the sample size calculation not conforming to clinical reality), the protocol should be revised, and the revision should be submitted to the ethics committee for approval.

15. Direct access to source data and files

Source data refers to all information in the original records of clinical findings, observations, and other activities in a clinical trial, as well as in their approved copies, which can be used for clinical trial reconstruction and evaluation. The source data for this trial includes: subject name, date of birth, and gender; case number and protocol number; trial enrollment date, date and method of use of experimental equipment; investigator's signature; adverse events/serious adverse events and their management; laboratory specimen collection date, result and reporting date, inspector's signature; monitor's signature; etc.

Source documents refer to printed, visual, or electronic documents containing source data . The source documents for this trial include: informed consent forms; subject screening and enrollment forms; subject identification coding forms; subject medical records (medical records, research medical records, physical and chemical examination reports); experimental

equipment usage records; laboratory records; adverse event/serious adverse event reporting forms, etc.

XVI. Finance and Insurance

The sponsor of the clinical trial is Hunan Haokang Medical Technology Co., Ltd., which will independently bear all financial responsibilities related to the trial, and there is no conflict of interest. Specific details and terms will be determined through agreements signed with each trial institution. For any injuries incurred during the trial related to the trial, the sponsor, Hunan Haokang Medical Technology Co., Ltd., will provide the corresponding costs for examination, treatment, and rehabilitation, and will also provide appropriate financial compensation.

XVII . Contents that should be included in a clinical trial report

Clinical trial personnel should fully understand the requirements of the trial and maintain complete and timely records throughout the clinical process to provide raw data for the clinical trial summary. Before the clinical trial begins, all materials and related documents should be prepared, including the clinical trial protocol, clinical trial agreement, case report forms, informed consent forms for subjects, investigator's brochure, etc. All records during the clinical trial, including case report forms, informed consent forms for subjects, and handover records of the investigational product, should be kept.

After the clinical trial concludes, the clinical trial personnel will prepare a "Medical Device Clinical Trial Report" for the product, which will be signed by the principal investigator of the clinical trial. Based on the actual situation of the clinical trial, the device will be discussed, and suggestions for improvement will be made regarding any problems encountered. Finally, a conclusion will be drawn regarding the clinical trial.

18. Principle of Confidentiality

Researchers must ensure the privacy of clinical trial participants is protected. In all documents submitted to the sponsor, participants should be identified only by their clinical trial number, and their names and hospital numbers should not be provided. Researchers must safeguard the names and addresses of clinical trial participants and the corresponding enrollment forms. These enrollment forms must be kept strictly confidential by the researchers and must not be submitted to the sponsor.

19. Agreement on the Publication of Test Results

After the trial concludes, the lead institution has the right to publish this clinical trial summary report in the form of a paper, with the first author and corresponding author being personnel from the lead institution; the principal investigators and sponsor representatives of each research institution have the right to be listed as authors on the paper.

20. Responsibilities of Each Party

(a) Responsibilities of the applicant

(1) Provide the medical institutions undertaking clinical trials with relevant clinical trial information as required by the state;

(2) Provide the trial product and related auxiliary supplies to the medical institutions undertaking the clinical trial free of charge;

(3) Responsible for providing relevant quality inspection certificates for the test products, and the conclusion should be qualified;

(4) Responsible for formulating product usage and operation specifications;

(5) Responsible for providing product usage training to clinical trial researchers;

(6) Provide clinical trial-related expenses to the medical institutions undertaking clinical trials;

(7) Collaborate with medical institutions undertaking clinical trials to complete clinical trial protocol design and data processing;

(8) Responsible for monitoring clinical trials;

(9) If the subject suffers harm due to the quality problem of the test product, the test product shall pay the relevant treatment costs and provide appropriate compensation.

(ii) Responsibilities of medical institutions undertaking clinical trials

(1) Understand and be familiar with the properties, effects, efficacy and safety of the test product;

(2) Possess the professional expertise, qualifications, and ability to undertake this clinical trial;

(3) Be familiar with the information and literature related to the clinical trial provided by the sponsor;

(4) They should be familiar with the relevant information provided by the sponsor and with the usage methods of the tested product;

(5) Jointly design and develop clinical trial protocols with the sponsor, and both parties sign the clinical trial protocol and contract;

(6) The investigator must read and understand the contents of the trial protocol in detail and strictly follow the relevant provisions of the protocol and the regulations for the management of clinical trials of medical devices. The investigator shall be responsible for the presentation and defense and the supplementation and modification of the trial data from the effective date of the agreement.

(7) The subject must be informed of the details of the test product. Before the clinical trial, the subject must be given sufficient time to consider whether to participate in the clinical trial.

(8) In the event of an adverse event, clinical trial personnel shall make a

timely clinical judgment and take measures to protect the interests of the subjects; if necessary, the ethics committee has the right to immediately suspend the clinical trial;

(9) If a clinical trial is terminated, the subjects, the sponsor, the ethics committee, and the provincial, autonomous region, or municipal (food) drug administration department and the State Food and Drug Administration that accepted the medical device registration application shall be notified, and the reasons shall be explained;

(10) Submit clinical trial reports and be responsible for the accuracy and reliability of the reports;

(11) Has an obligation to keep confidential the information provided by the applicant;

(12) When adverse reactions occur, appropriate treatment measures should be taken for the subjects immediately, and the report should be made to the drug regulatory authority, the sponsor, the ethics committee and all participating clinical trial units, and the report should be signed and dated;

(13) Accurately, completely, promptly, and legally record information in medical record forms and test record books;

(14) With the consent of Party A, relevant experimental research papers may be published on the materials provided by Party A (the

applicant).

Researcher's Statement

I agree:

1. This clinical trial was conducted in strict accordance with the Declaration of Helsinki, current Chinese regulations, and the trial protocol.

2. Accurately record all required data in the Case Report Form (CRF) and complete the clinical trial report on time.

3. The investigational medical device shall be used only in this clinical trial. The receipt and use of the investigational medical device shall be recorded completely and accurately during the clinical trial, and the records shall be preserved.

4. Allow monitors, inspectors, and regulatory authorities authorized or dispatched by the sponsor to monitor, inspect, and examine the clinical trial.

5. Strictly adhere to the terms of the clinical trial contracts/agreements signed by all parties.

I have read the entire clinical trial protocol, including the above statements, and I agree to all of the above.

Applicant's Opinion Signature (or stamp) Date

Researchers' opinions sign Date

Opinions of Medical Device Clinical Trial Institutions   Signature (or stamp) Date

Appendix 1 - Quality of Life Survey

Quality of life survey

serial number_

We are eager to understand your health and quality of life. Please answer the following questions and circle the answer that best suits you. There are no "right" or "wrong" answers to these questions. All information you provide will be kept strictly confidential.

	No	Slightly	quite	Very
1. Do you find it difficult when you do strenuous tasks, such as carrying heavy shopping bags or suitcases?				
2. Do you find long walks difficult?				
3. Do you find it difficult to take short walks outdoors?				
4. Do you spend most of your day in bed or sitting in a chair?				
5. Do you need assistance with eating, dressing, bathing, or using the toilet?				
6. Are your work or daily activities restricted?				

7. Do you feel restricted in your favorite or other leisure activities?				
8. Have you ever experienced shortness of breath?				
9. Do you experience any pain?				
10. Have you ever needed a break?				
11. Do you have trouble sleeping?				
12. Have you ever felt weak?				
13. Have you ever experienced a lack of appetite?				
14. Have you ever felt nauseous?				
15. Have you ever vomited?				
16. Have you ever suffered from constipation?				
17. Have you ever had diarrhea?				
18. Do you feel tired?				
19. Does the pain interfere with your daily activities?				
20. Do you have difficulty concentrating on tasks, such as reading a newspaper or watching television?				
21. Have you ever felt nervous?				
22. Are you worried?				
23. Do you feel irritable?				
24. Do you feel depressed?				
25. Do you have difficulty remembering things?				
26. Is your health condition or treatment interfering with your family life?				
27. Does your physical condition or treatment interfere with your				

social activities?				
28. Is your health condition or treatment causing you financial hardship?				

For the following questions, please circle the number that best suits you between 1 and 7.

29. How would you rate your overall health over the past week?

1 2 3 4 5 6 7

Very bad Excellent

30. How would you rate your overall quality of life over the past week?

1 2 3 4 5 6 7

Very bad Excellent

Appendix 2 - Researcher Equipment Experience Survey

Researcher Equipment Experience Survey Form No._____

Experience Project	Details	User experience review	Encountering problems	Suggestions for improvement
Instrument appearance and design	Structural design	A. Good B. Fair C. Average D. Poor E. Poor		
	Packaging	A. Good B. Fair C. Average D. Poor E. Poor		
	Physicochemical properties	A. Good B. Fair C. Average D. Poor E. Poor		
	Appearance	A. Good B. Fair C. Average D. Poor E. Poor		

	Quality stability	A. Good B. Fair C. Average D. Poor E. Poor		
	Model Identification	A. Good B. Fair C. Average D. Poor E. Poor		
Equipment usage	Install	A. Good B. Fair C. Average D. Poor E. Poor		
	Insert	A. Good B. Fair C. Average D. Poor E. Poor		
	take out	A. Good B. Fair C. Average D. Poor E. Poor		
Overall satisfaction	A. Good B. Fair C. Average D. Poor E. Poor			
Content upgrade	How would you like to further upgrade your uterine stent?			
	What is your overall evaluation and personal recommendation of uterine stents?			
Medical device prices	Your estimated price			

Appendix 3 - References

References

[1] Surgery AE G. AAGL practice report: practice guidelines on intrauterine adhesion developed in collaboration with the European Society of Gynecological Endoscopy (ESGE):[J]. Gynecological Surgery, 2017, 14(1):6.

[2] Obstetrics and Gynecology Branch of Chinese Medical Association. Chinese expert consensus on clinical diagnosis and treatment of intrauterine adhesions [J]. Chinese Journal of Obstetrics and Gynecology, 2015, 50(12):881-887.

[3] Salma U, Xue M, Md Sayed AS, et al. Efficacy of intrauterine device in the treatment of intrauterine adheions.[J]. Biomed Research International, 2014, 2014(2014):589296.

[4] Xiao Songshu, Wan Yajun , Zou Fangjun, Ye Mingzhu, Deng Henan, Ma Jiezhi, Wei Yingying, Tan Chen, Xue Min . A prospective , randomized, negative-controlled clinical study on the prevention of re-adhesion after separation surgery for moderate to severe intrauterine adhesions using self-crosslinked sodium hyaluronate gel [J]. Chinese Journal of Obstetrics and Gynecology, 2015, 50(1).

[5] Wei Minling, Lin Xiaona, Zhou Feng, Huang Dong, Kuang Lin, Zhang Songying. Safety and patient acceptance evaluation of uterine balloon stent for the prevention of intrauterine adhesions [J]. Chinese Medical Journal, 2014, 94(39).

[6] Zhu Leilei, Feng Shuying, Zhang Xin, Chen Libin, Zhang Xiaolan, Li Yuzhu. Clinical application of long-term placement of Cook balloon stent in preventing recurrence of intrauterine adhesions after surgery [J]. China Modern Drug Application, 2016, 10(6).

[7] Wang Xiuqin, Xiong Ningning, Liu Fang, Jiang Meng, Zou Jiandong, Fu Weimin, Xue Xuekun. Risk assessment and safety monitoring in clinical trials [J]. Chinese Journal of New Drugs. 2005, 14(6).

[8] Zhou Jingwei. Research on the biocompatibility and physical and mechanical properties of PU material intrauterine devices [D]. Central South University, 2014.

[9] Xu Junlei. Study on the safety of uterine-shaped silicone intrauterine adhesion treatment device on goat endometrium [D]. Central South University, 2013

[10] Li Bo. Biocompatibility Study of Intrauterine Adhesion Treatment Device [D]. Central South University, 2011.