Bayer IUDs (Intrauterine Devices): An Overview

Mirena® (levonorgestrel-releasing intrauterine system) 52mg

Kyleena® (levonorgestrel-releasing intrauterine system) 19.5mg

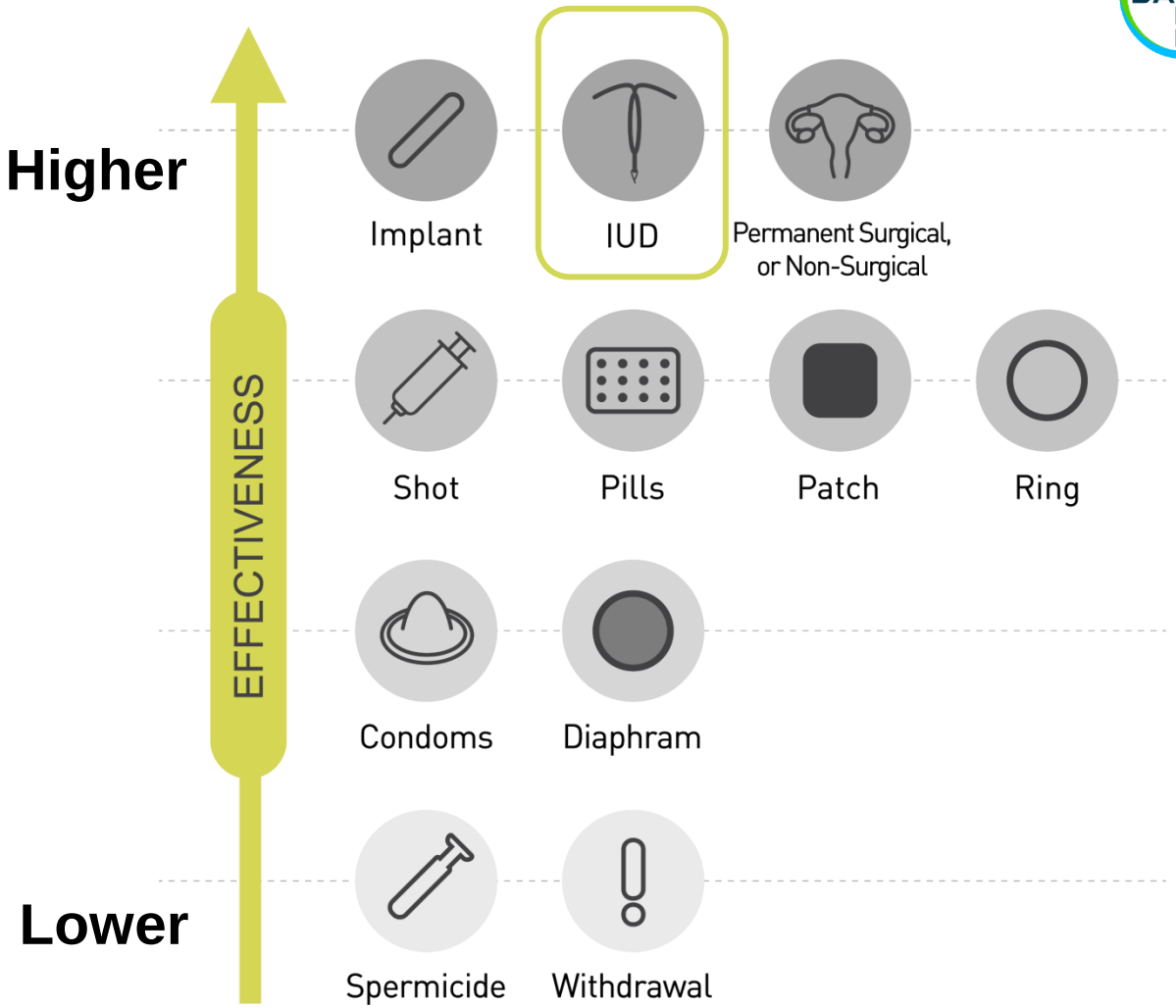
Skyla® (levonorgestrel-releasing intrauterine system) 13.5mg

Please see Important Safety Information throughout. Please see full Prescribing Information for Mirena, Kyleena, and Skyla that is available at this presentation.

PP-PF-WHC-IUS-US-1647-1, May 2023

Contraceptive Options

An Intrauterine Device (IUD) is a long acting method of birth control, and is considered to be one of the most effective methods of reversible birth control[1]



[1] Obstet Gynecol. 2017 Nov;130(5):e251-e269

What are Mirena, Kyleena, & Skyla?

Indications

Mirena® (levonorgestrel-releasing intrauterine system) 52 mg

- Prevention of pregnancy for up to 8 years; replace after the end of the eighth year
- Treatment of heavy menstrual bleeding for up to 5 years in women who choose to use intrauterine contraception as their method of contraception; replace after the end of the fifth year if continued treatment of heavy menstrual bleeding is needed

Kyleena® (levonorgestrel-releasing intrauterine system) 19.5 mg

- Prevention of pregnancy up to 5 years
- Replace the system after 5 years if continued use is desired

Skyla® (levonorgestrel-releasing intrauterine system) 13.5 mg

- Prevention of pregnancy up to 3 years
- Replace the system after 3 years if continued use is desired

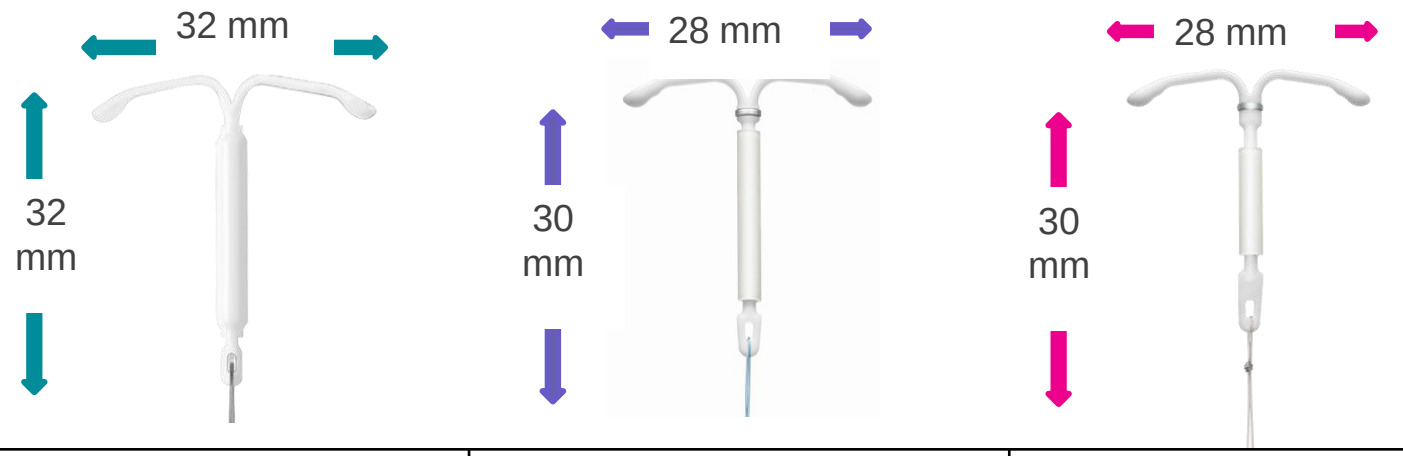
Please see Important Safety Information throughout. Please see full Prescribing Information for Mirena, Kyleena, and Skyla that is available at this presentation.

Properties

Mirena® (levonorgestrel-releasing intrauterine system) 52 mg

Kyleena® (levonorgestrel-releasing intrauterine system) 19.5 mg

Skyla® (levonorgestrel-releasing intrauterine system) 13.5 mg



Hormone Reservoir (Total Amount)	52mg LNG	19.5mg LNG	13.5mg
Insertion Tube Diameter	4.4 mm	3.8 mm	3.8mm
Release Rate After 1 Year	19 mcg/d	9.8 mcg/d	~6 mcg/d
Thread color	Brown	Blue	Brown
Silver Ring / MR Compatibility	No Silver Ring	Yes / MR Conditional	Yes / MR Conditional

The combination of silver ring and thread color will help identify the brand of IUD.

Please see Important Safety Information throughout. Please see full Prescribing Information for Mirena, Kyleena, and Skyla that is available at this presentation.

Important Safety Information

Contraindications

- Known or suspected pregnancy and cannot be used for post-coital contraception
- Congenital or acquired uterine anomaly including fibroids if they distort the uterine cavity
- Known or suspected breast cancer or other progestin-sensitive cancer, now or in the past
- Known or suspected uterine or cervical malignancy
- Liver disease, including tumor
- Untreated acute cervicitis or vaginitis, including lower genital tract infections (e.g. bacterial vaginosis) until infection is controlled
- Postpartum endometritis or infected abortion in the past 3 months
- Unexplained uterine bleeding
- Current IUD
- Acute pelvic inflammatory disease (PID) or a history of PID (except with later intrauterine pregnancy)
- Conditions increasing susceptibility to pelvic infections
- Hypersensitivity to any component of the Mirena, Kyleena, or Skyla

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Important Safety Information

Clinical Considerations for Use and Removal

Use Mirena, Kyleena or Skyla with caution after careful assessment in patients with:

- Coagulopathy or taking anticoagulants
- Migraine, focal migraine with asymmetrical visual loss, or other symptoms indicating transient cerebral ischemia
- Exceptionally severe headache
- Marked increase of blood pressure, or
- Severe arterial disease such as stroke or myocardial infarction

- Consider removing the intrauterine system if these or the following arise during use: Uterine or cervical malignancy or jaundice
- If the threads are not visible or are significantly shortened they may have broken or retracted into the cervical canal or uterus
- If Mirena, Kyleena, or Skyla is displaced (e.g. expelled or perforated the uterus) remove it
- Kyleena and Skyla can be safely scanned with MRI only under specific conditions

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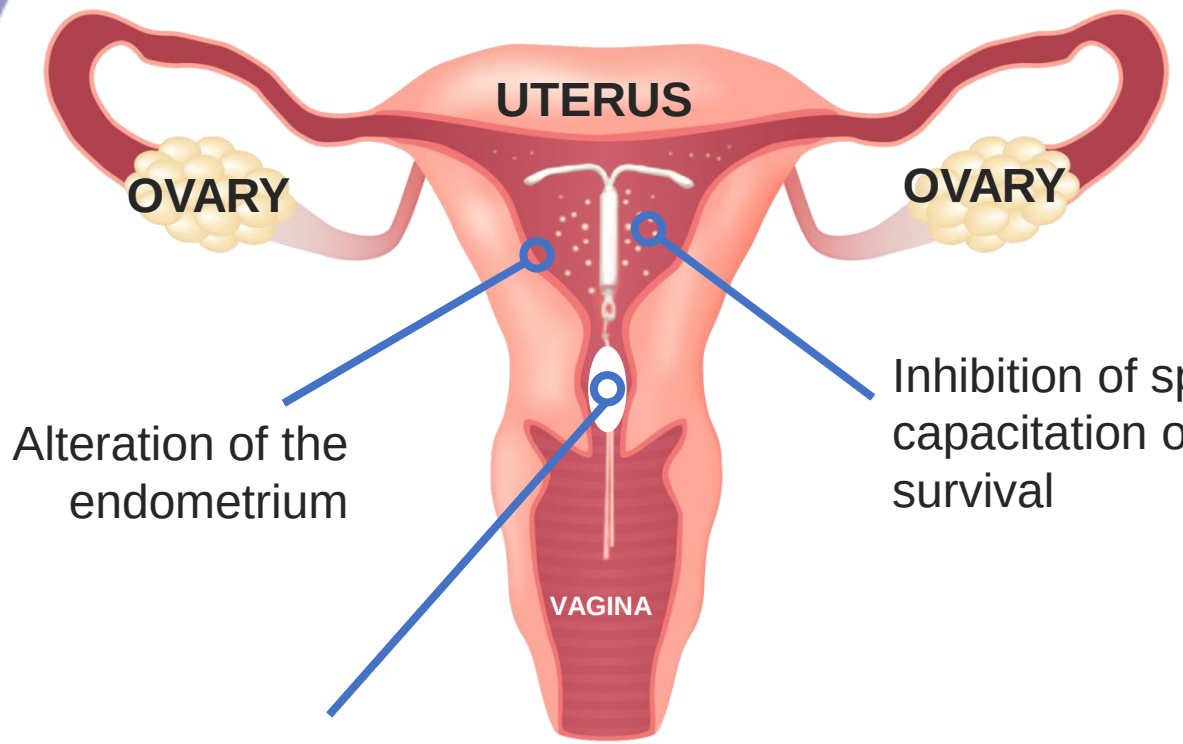
Suggested Mechanism of Action

The local mechanism of action has not been conclusively demonstrated.

Studies of Mirena, Kyleena, Skyla and similar LNG-IUS prototypes have suggested several mechanisms that may prevent pregnancy.



Thickening of cervical mucus (CM) preventing passage of sperm into the uterus

(*click to view an example of thickened CM from LNG-IUS user*)

Efficacy

Mirena® (levonorgestrel-releasing intrauterine system) 52 mg | Kyleena® (levonorgestrel-releasing intrauterine system) 19.5 mg | Skyla® (levonorgestrel-releasing intrauterine system) 13.5 mg

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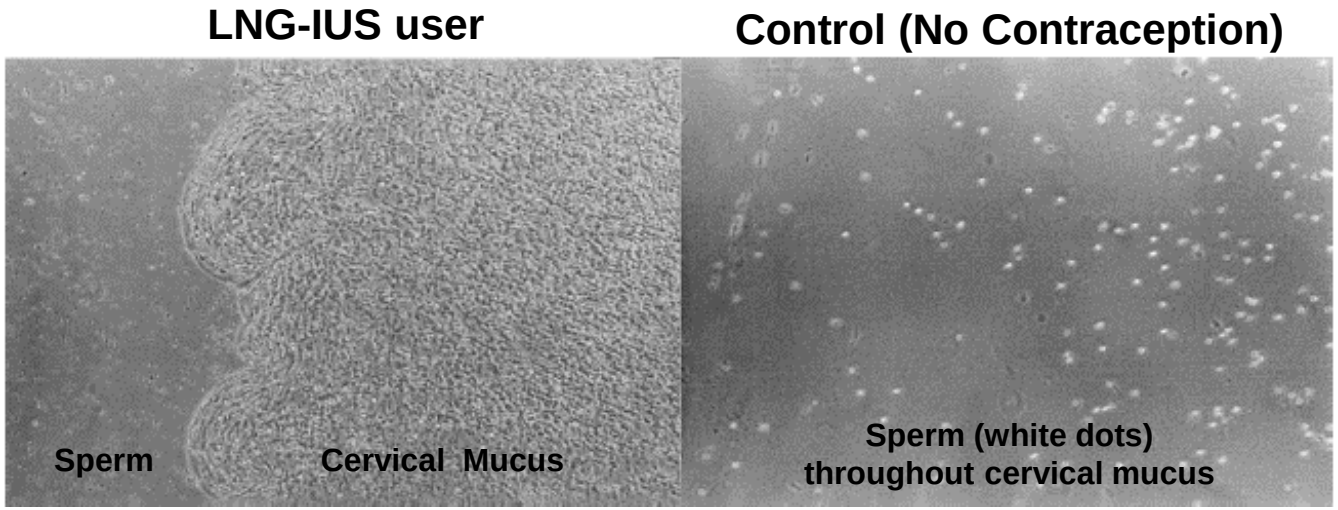
Cervical Mucus Changes During LNG-IUS Use

The local mechanism of action has not been conclusively demonstrated. Thickening of cervical mucus is one of the several suggested mechanisms that may prevent pregnancy.

These examples show how cervical mucus from an LNG-IUS user is thick, compared to a control patient (not using contraception).

Examples of Cervical Mucus



Lewis et al., 2010. Used with permission.

- Mid-cycle Cervical Mucus (CM) from LNG-IUS user (left) and control patient (right) were placed on slide and surrounded by sperm.
- Sperm are unable to penetrate CM from LNG-IUS user, but swim throughout control CM

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Mirena®
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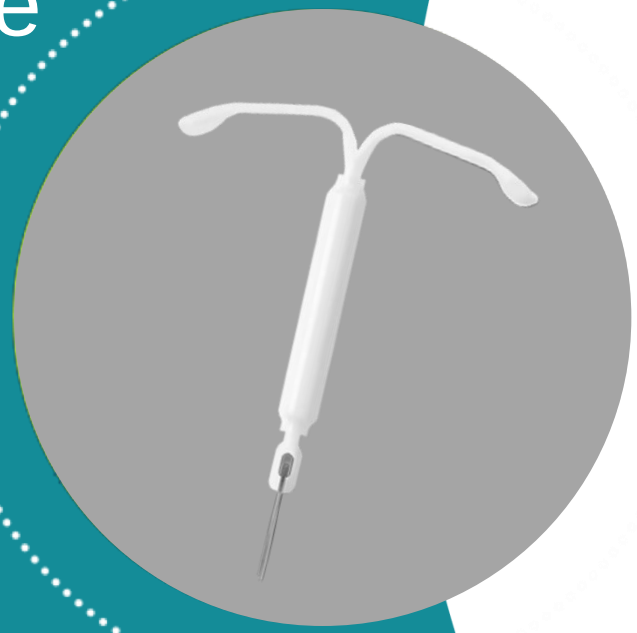
Contraceptive Efficacy

Contraception Clinical Trials



5 Year Trial: conducted in Finland & Sweden

Extension Trial: multi-center, open label, uncontrolled study in the US

Please see Important Safety Information throughout. Please see full Prescribing Information for Mirena, Kyleena, and Skyla that is available at this presentation.

BAYER

5-Year Trial

- N=1,169 women (18-35 years old)
- 5.6% nulliparous (n=66)
- 1-year pregnancy rate ≤0.2/100 women (0.2%)
- 5-year cumulative pregnancy rate ~0.7/100 women (0.7%)

Extended Use Beyond 5 Years

- N=362 women (18-35 years old) using Mirena for 4.5-5years
- 47.2% nulliparous
- BMI range: 15.4-57.7 kg/m^2 (avg=27.9 kg/m^2)
- Pearl index: 0.34 (year 6), 0.40 (year 7), 0.00 (year 8)
- 3-year cumulative pregnancy rate (years 6-8) = 0.68% (95% Upper Confidence limit = 2.71%)

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Mirena® (levonorgestrel-releasing intrauterine system) 52 mg

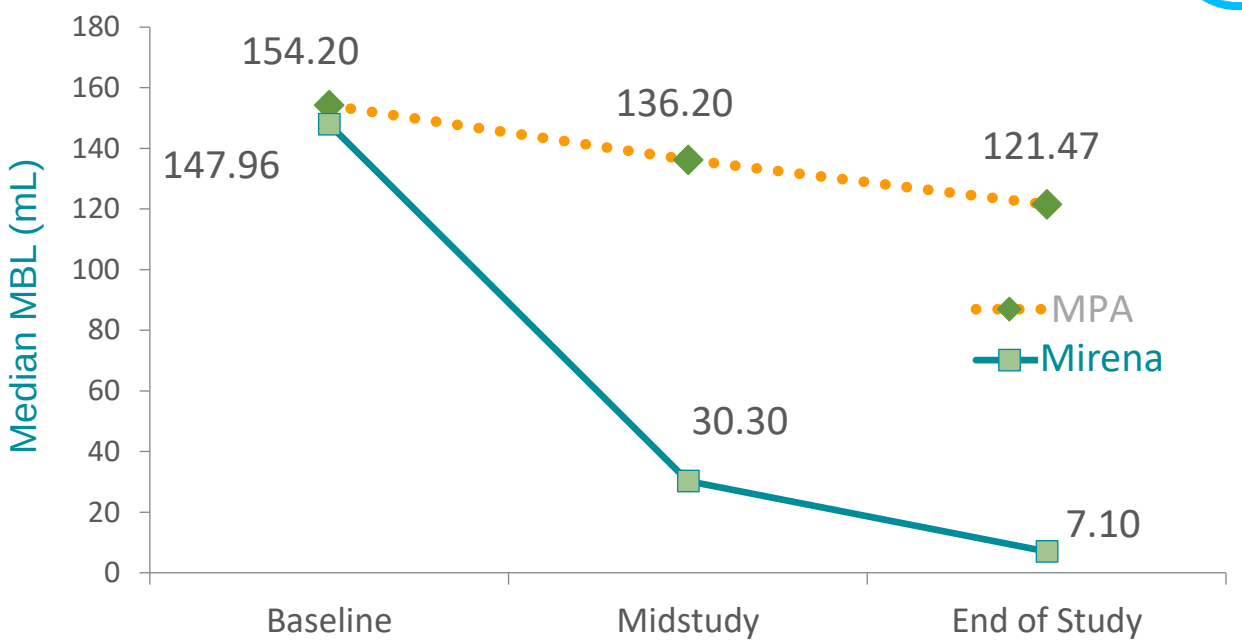
Clinical Trial on Heavy Menstrual Bleeding

Trial Overview[1,2]:

Randomized, open label, active control, parallel group trial of reproductive aged women with ≥80 mL menstrual blood loss (MBL)* confirmed with alkaline hematin method[1,2]

Women were randomized to 6 cycles of Mirena (n=79) or Medroxyprogesterone acetate (MPA) (n=81) 10 mg/day for 10 days beginning on day 16 of cycle[1,2]

*Excluded were women with organic or systemic conditions that may cause heavy uterine bleeding



Mirena, users demonstrated:
80% reduction in the median MBL at 3 cycles
95% reduction in the median MBL at 6 cycles

Please see Important Safety Information throughout. Please see full Prescribing Information for Mirena, Kyleena, and Skyla that is available at this presentation.

[1] Mirena Prescribing Information [2] Kaunitz AM, et al. Obstet Gynecol. 2010;116:625–32

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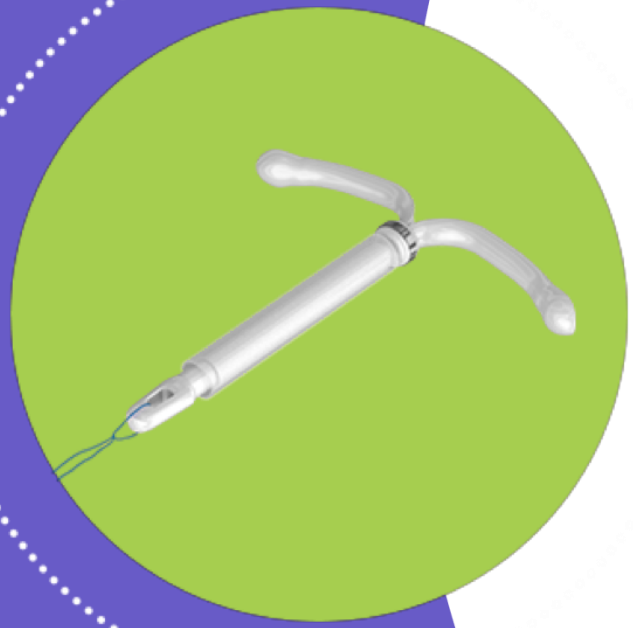
Contraceptive Efficacy

Contraception Clinical Trials



Multicenter, multi-national, randomized, open-label study conducted in 11 countries including the USA

Demographics	**N=1,452 women (5 year trial)** • 18-35 years • 40% nulliparous (n=574) • BMI range: 15.2-57.6 kg/m^2 (avg=25.3 kg/m^2)
Efficacy	• Year 1 Pearl Index= 0.16 • Cumulative 5-year pregnancy rate = 1.45% (95% Confidence Interval: 0.82, 2.53)

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Skyla®
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Contraceptive Efficacy

Contraception Clinical Trials

Multicenter, multi-national, randomized, open-label study conducted in 11 countries including the USA

Demographics	**N=1,432 women (3 year trial)** • 18-35 years • 38.8% nulliparous (n=556) • BMI range: 16-55 kg/m^2 (avg=25.3 kg/m^2)
Efficacy	• Year 1 Pearl Index= 0.41 • Cumulative 3-year pregnancy rate = 0.9% (upper 95% Confidence Interval: 1.7%)

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Important Safety Information

Pregnancy Related Risks

- If pregnancy should occur with Mirena, Kyleena, or Skyla in place, remove the intrauterine system because leaving it in place may increase the risk of spontaneous abortion and preterm labor.
- Advise her of isolated reports of virilization of the female fetus following local exposure to LNG during pregnancy with an LNG-IUS in place
- Removal or manipulation may result in pregnancy loss.
- Evaluate women for ectopic pregnancy because the likelihood of a pregnancy being ectopic is increased with Mirena, Kyleena, or Skyla.
- Also consider the possibility of ectopic pregnancy in the case of lower abdominal pain, especially in association with missed menses or if an amenorrheic woman starts bleeding.
- Tell women about the signs of ectopic pregnancy and associated risks, including loss of fertility.
- Women with a history of ectopic pregnancy, tubal surgery, or pelvic infection carry a higher risk of ectopic pregnancy

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Insertion Timing

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Kyleena® (levonorgestrel-releasing intrauterine system) 19.5mg

Skyla® (levonorgestrel-releasing intrauterine system) 13.5mg

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Timing of Insertion

Consider same day insertion if there is reasonable certainty the patient is not pregnant

	Insertion timing	Backup contraception?
Patients not currently using hormonal or intrauterine contraception	• Any time there is reasonable certainty that they are not pregnant • Consider the possibility of ovulation and conception prior to initiation	**YES** if not inserted during the first 7 days of the menstrual cycle, a barrier method should be used or patient should abstain from vaginal intercourse for 7 days **NO** If inserted during the first 7 days of the menstrual cycle, or immediately after first trimester abortion
Switching from:		
Oral, transdermal, or vaginal hormonal contraceptive	• Any time, including the hormone-free interval of the previous method	**YES** if inserted during active use of previous method, continue that method for 7 days after insertion, or until the end of the current treatment cycle **YES** if inserted during use of continuous hormonal contraception, discontinue method 7 days after insertion
Injectable progestin contraceptive	• Any time	**YES** if inserted>3 months (13 weeks) after the last injection, non-hormonal back-up birth control (such as condoms or spermicide) should also be used for 7 days **NO** if inserted <3 months after last injection
Implant or another IUS	• Anytime during the menstrual cycle • Insert the IUD on the same day the implant or IUS is removed	**NO** there is no need for backup contraception

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Timing of Insertion

After First or Second Trimester Abortion or miscarriage, and Childbirth

	Insertion timing	Backup contraception?
After 1st trimester abortion or miscarriage	• Can be inserted immediately, unless it's a septic abortion	**NO** There is no need for backup contraception
After childbirth or 2nd trimester abortion or miscarriage		
Immediate insertion after childbirth, or 2nd trimester abortion or miscarriage	• Insert after removal of placenta	**NO** There is no need for backup contraception
Interval insertion following complete involution of the uterus	• Wait a minimum of 6 weeks, or until the uterus is fully involuted before insertion • Insert any time there is reasonable certainty that the patient is not pregnant	**YES** If not inserted during the first 7 days of the menstrual cycle, a back-up method of contraception should be used, or the patient should abstain from vaginal intercourse for 7 days **NO** If inserted during the first 7 days of the menstrual cycle

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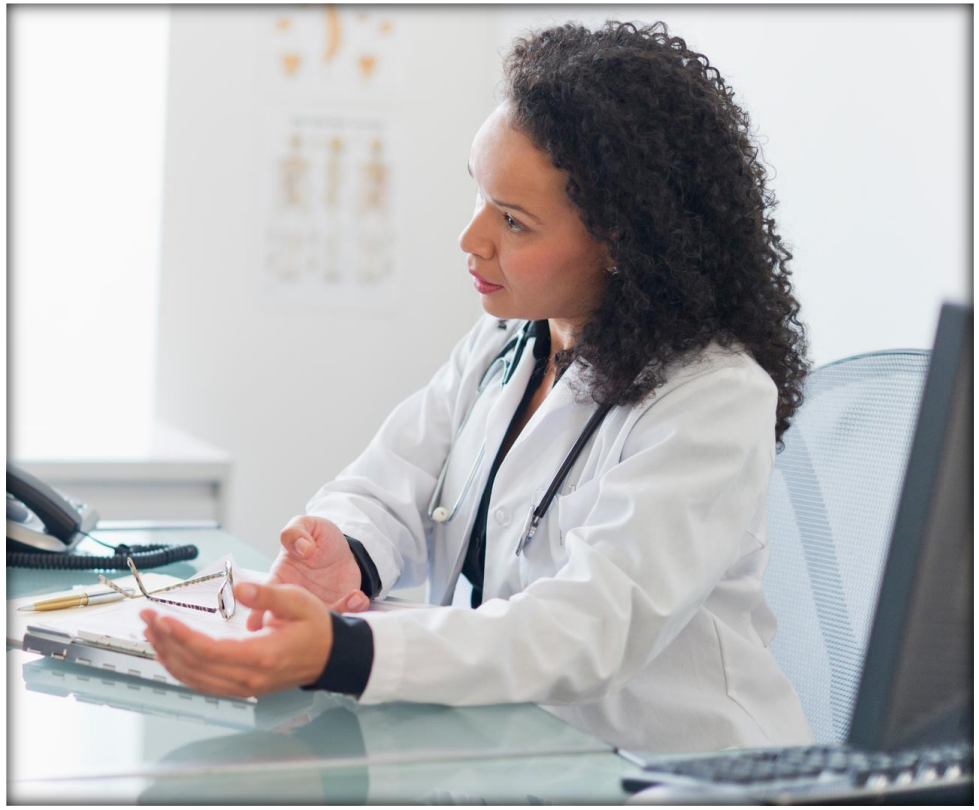
Insertion Pain

- Patients may experience pain, bleeding or dizziness during and after placement.
- If symptoms do not pass within 30 minutes, the Bayer IUD may not have been placed correctly.
- If this happens, the patient should be examined to determine if the Bayer IUD needs to be removed or replaced.



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Kyleena: Data on Pain at Insertion[1]

- **Study Design**: prospective, non-interventional, multinational, single arm cohort study
- **Study Evaluations:** Pain at insertion was a secondary endpoint*, assessed using the categories none, mild, moderate, or severe.
- **Participants**:
  - Were approached about the study after they decided to use Kyleena
  - Included patients switching from different contraceptive methods, and those without or any prior contraceptive method use

*Overall satisfaction with Kyleena was the primary endpoint by country and by previously used contraceptive method

1. Beckert, V et al, Eur J Contracept Reprod Health Care 2020 Jun;25(3):182-189. Epub 2020 Mar 30

Kyleena® (levonorgestrel-releasing intrauterine system) 19.5 mg

Kyleena: Data on Pain at Insertion[1]

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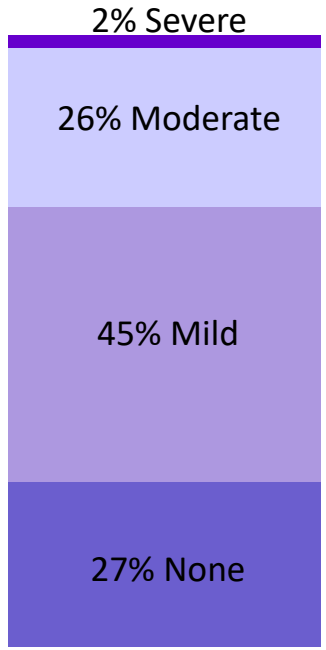
- **Study Evaluations:** Pain at insertion was a secondary endpoint*, assessed using the categories none, mild, moderate, or severe.
- **Participants**:
  - Were approached about the study after they decided to use Kyleena
  - Included patients switching from different contraceptive methods, and those without or any prior contraceptive method use
- **Additional Pain Control Measures used at Insertion:**
  - 88% of insertions did not require additional pain control measures
  - 2% used local analgesia,
  - 4% used systemic analgesia (e.g. NSAID),
  - 6% used both local and systemic analgesia

Among the 100 Participants from 12 US sites:



Patient's Assessment of Pain at Insertion

*Overall satisfaction with Kyleena was the primary endpoint by country and by previously used contraceptive method

1. Beckert, V et al, Eur J Contracept Reprod Health Care 2020 Jun;25(3):182-189. Epub 2020 Mar 30

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Kyleena® (levonorgestrel-releasing intrauterine system) 19.5 mg

Important Safety Information

Educate her about Pelvic Inflammatory Disease (PID)

- Mirena, Kyleena, and Skyla are contraindicated in the presence of known or suspected PID or in women with a history of PID unless there has been a subsequent intrauterine pregnancy
- IUDs have been associated with an increased risk of PID, most likely due to organisms being introduced into the uterus during insertion. Promptly examine users with complaints of lower abdominal pain or pelvic pain, odorous discharge, unexplained bleeding, fever, genital lesions or sores
- Inform women about the possibility of PID and that PID can cause tubal damage leading to ectopic pregnancy or infertility, or infrequently can necessitate hysterectomy, or cause death

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Important Safety Information

Educate her about Pelvic Inflammatory Disease (PID) (cont.)

- PID is often associated with sexually transmitted infections (STIs); Mirena, Kyleena, and Skyla do not protect agains STIs, including HIV. PID may be asymptomatic but still result in tubal damage and its sequelae

- In clinical trials with:

    - **Mirena** – upper genital infections, including PID, occurred more frequently within the first year. In a clinical trial with other IUDs and a clinical trial with an IUD similar to Mirena, the highest rate occurred within the first month after insertion.

    - **Kyleena –** PID occurred more frequently within the first year and most often within the first month after insertion

    - **Skyla** – PID occurred more frequently within the first year and most often within the first month after insertion

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Effect on Bleeding

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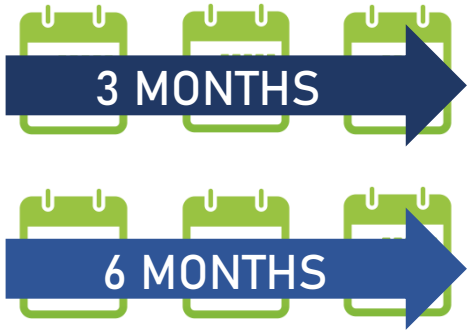
Important Safety Information

Expect changes in bleeding patterns



- Spotting and irregular or heavy bleeding may occur during the first 3 to 6 months
- Periods may become shorter and/or lighter thereafter. Cycles may remain irregular, become infrequent, or even cease

- Consider pregnancy if menstruation does not occur within 6 weeks of the onset of previous menstruation
- If a significant change in bleeding develops during prolonged use, take appropriate diagnostic measures to rule out endometrial pathology

Click here for more information on bleeding patterns with Mirena, Kyleena, and Skyla

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Other serious complications and most common adverse reactions

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Important Safety Information

Be aware of other serious complications and most common adverse reactions. Some serious complications with IUDs like Mirena, Kyleena, and Skyla are sepsis, perforation and expulsion.

SEPSIS:

- Severe infection, or sepsis, including Group A streptococcal sepsis (GAS), have been reported following insertion of a LNG-releasing IUS
- Aseptic technique during insertion of the IUD is essential in order to minimize serious infections such as GAS

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Important Safety Information

Be aware of other serious complications and most common adverse reactions (cont.):

PERFORATION:

- Perforation (total or partial, including penetration/embedment of Mirena, Kyleena, or Skyla in the uterine wall or cervix) may occur, most often during insertion, although the perforation may not be detected until sometime later.

- The risk of uterine perforation is increased in women who have recently given birth, and in women who are breastfeeding at the time of insertion.
  - In a large US retrospective, postmarketing safety study of IUDs, the risk of uterine perforation was highest when insertion occurred within ≤6 weeks postpartum, and also higher with breastfeeding at the time of insertion.

- The risk of perforation may be increased if inserted when the uterus is fixed, retroverted or not completely involuted.

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Important Safety Information

Be aware of other serious complications and most common adverse reactions (cont.):

PERFORATION:

- If perforation occurs, locate and remove the intrauterine system.
  - Surgery may be required.
  - Delayed detection or removal of the intrauterine system in case of perforation may result in migration outside the uterine cavity, adhesions, peritonitis, intestinal perforations, intestinal obstruction, abscesses, and erosion of adjacent viscera
- In addition, perforation may reduce contraceptive efficacy

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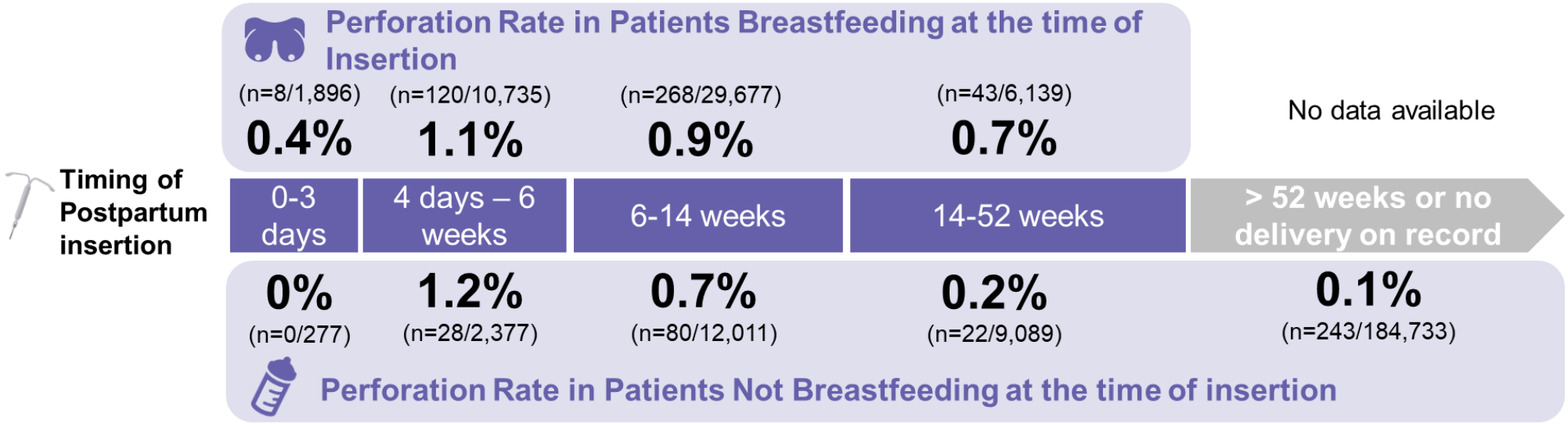
APEX-IUD Study

Assessment of Perforation and Expulsion of Intrauterine Devices Study

Purpose: retrospective cohort study (>320,000 IUD insertions) to assess the impact of breastfeeding (BF) and insertion timing on perforation and expulsion



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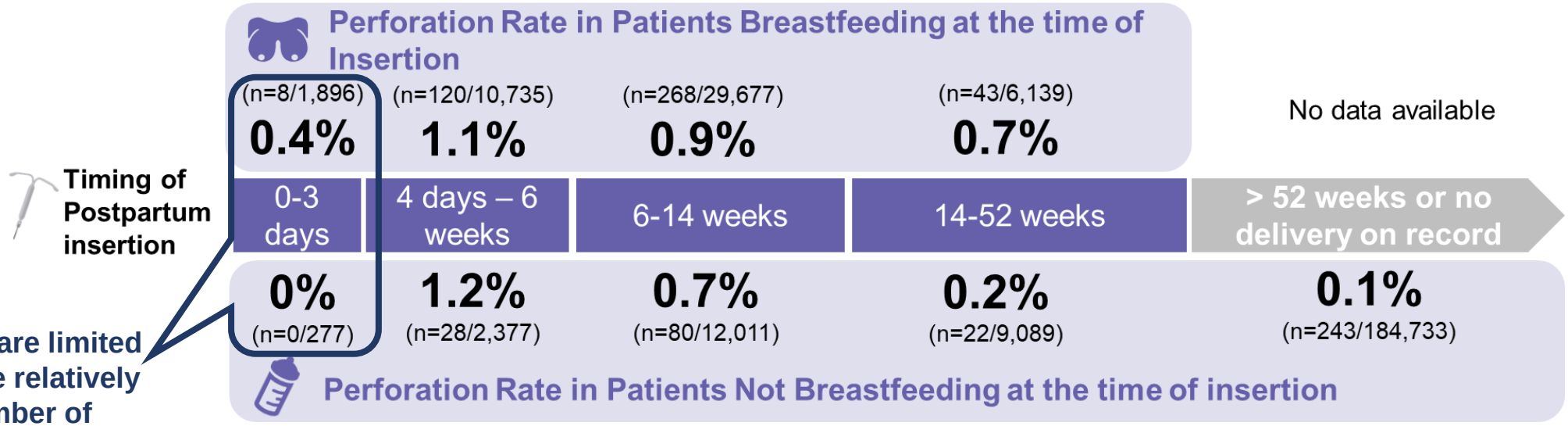
Assessment of Perforation and Expulsion of Intrauterine Devices Study

Purpose: retrospective cohort study (>320,000 IUD insertions) to assess the impact of breastfeeding (BF) and insertion timing on perforation and expulsion



Perforation Results:

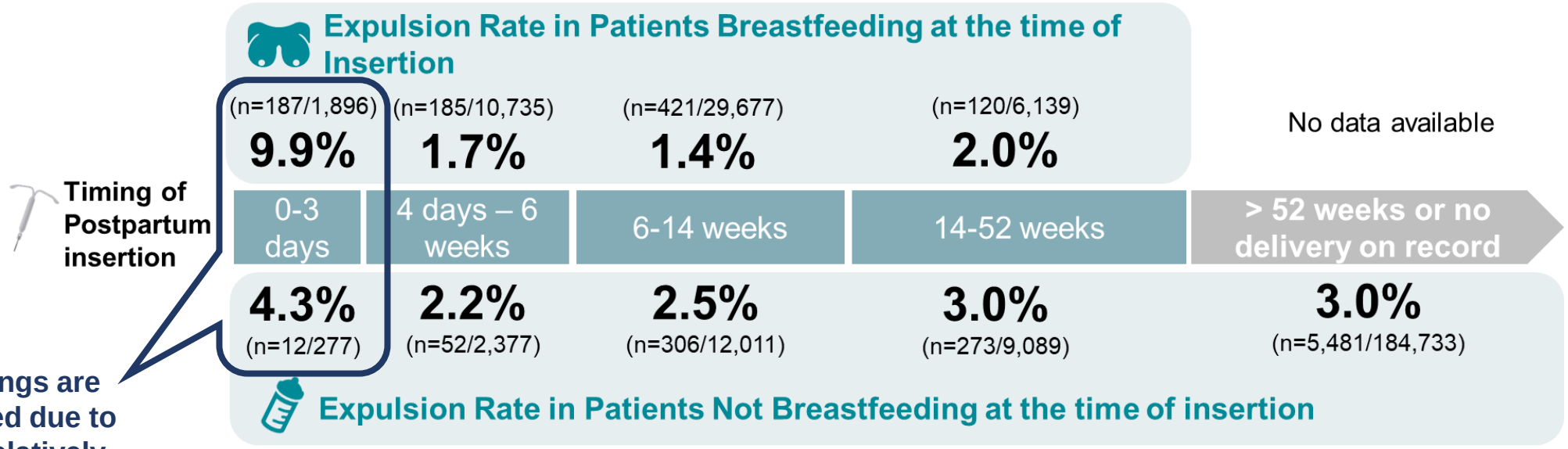
- Perforation rate was highest when IUDs were placed between 4 days-6 weeks after delivery
- Breastfeeding (vs. non) at the time of insertion was associated with a 33% higher risk of perforation (adjusted hazard ratio [HR]=1.33, 95% confidence interval [CI]: 1.07-1.64)

Please see Important Safety Information throughout. Please see full Prescribing Information for Mirena, Kyleena, and Skyla that is available at this presentation.

Mirena® (levonorgestrel-releasing intrauterine system) 52 mg | Kyleena® (levonorgestrel-releasing intrauterine system) 19.5 mg | Skyla® (levonorgestrel-releasing intrauterine system) 13.5 mg

APEX-IUD Study (cont.)

Assessment of Perforation and Expulsion of Intrauterine Devices Study



Findings are limited due to the relatively small number of insertions during this time

Expulsion Results:

- Risk of expulsion was variable over the postpartum intervals through 52 weeks, and highest when the LNG-IUS was placed the first 3 days after delivery
- Breastfeeding (vs. non) at the time of insertion was associated with a 28% lower risk of expulsion (adjusted hazard ratio [HR]=0.72, 95% confidence interval [CI]: 0.64-0.80)

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Important Safety Information

Be aware of other serious complications and most common adverse reactions (cont.):

EXPULSION:

- Partial or complete expulsion of Mirena, Kyleena, or Skyla may occur resulting in the loss of contraceptive protection.
- The risk of expulsion is increased with insertions immediately after delivery and appears to be increased with insertion after second-trimester abortion based on limited data.
- In the same postmarketing study, the risk of expulsion was lower with breastfeeding status.
- Remove a partially expelled IUD.
- If expulsion has occurred, a new Mirena, Kyleena, or Skyla can be inserted any time the provider can be reasonably certain the woman is not pregnant.

OVARIAN CYSTS:

- Ovarian cysts may occur and are generally asymptomatic, but may be accompanied by pelvic pain or dyspareunia
- Evaluate persistent enlarged ovarian cysts

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Be aware of other serious complications and most common adverse reactions (cont.): In clinical trials with:

Mirena – adverse reactions reported in ≥5% of users were:			
Alterations in menstrual bleeding patterns Unscheduled uterine bleeding Decreased uterine bleeding Increased scheduled uterine bleeding Female genital tract bleeding	 31.9% 23.4% 11.9% 3.5%	Breast pain	8.5%
Abdominal/pelvic pain	22.6%	Back pain	7.9%
Amenorrhea	18.4%	Benign ovarian cyst and associated complications	7.5%
Headache/migraine	16.3%	Acne	6.8%
Genital discharge	14.9%	Depression/depressive mood	6.4%
Vulvovaginitis	10.5%	Dysmenorrhea	6.4%

A separate study with 362 women who have used Mirena for more than 5 years showed a consistent adverse reaction profile in years 6 - 8. By the end of Year 8 of use:

- amenorrhea and infrequent bleeding were experienced by 34% and 26% of users, respectively;
- irregular bleeding occurs in 10%,
- Frequent bleeding occurs in 3%, and
- prolonged bleeding in 3% of users.

In this study, 9% of women reported the adverse event of weight gain, it is unknown if the weight gain was caused by Mirena.

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Important Safety Information

Be aware of other serious complications and most common adverse reactions (cont.):

Kyleena – the most common adverse reactions (≥5% users) were:	
Vulvovaginitis	24%
Ovarian Cyst	22%
Abdominal/pelvic pain	21%
Headache/migraine	15%
Acne/seborrhea	15%
Dysmenorrhea/uterine spasm	10%
Breast pain/discomfort	10%
Increased bleeding	8%

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Important Safety Information

Be aware of other serious complications and most common adverse reactions (cont.): In clinical trials with:

Skyla – the most common adverse reactions (≥5% users) were:	
Vulvovaginitis	20.2%
Abdominal/pelvic pain	18.9%
Acne/seborrhea	15.0%
Ovarian cyst	13.2%
Headache	12.4%
Dysmenorrhea	8.6%
Breast pain/discomfort	8.6%
Increased bleeding	7.8%
Nausea	5.5%

Teach patients to recognize and immediately report signs or symptoms of the aforementioned conditions. Evaluate patients 4 to 6 weeks after insertion of Mirena, Kyleena, and Skyla and then yearly or more often if clinically indicated

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Confirm your attendance

Please visit – IUDTraining.com to receive

A certificate of attendance

Access to additional educational resources, support, and follow-up from Bayer Representatives

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Insertion & Removal

Mirena® (levonorgestrel-releasing intrauterine system) 52mg

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Skyla® (levonorgestrel-releasing intrauterine system) 13.5mg

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Insertion Procedure

- Obtain a complete medical and social history to determine conditions that might influence selection of a Bayer IUD for contraception
    - If indicated, perform a physical examination, and appropriate tests for any forms of genital or other sexually transmitted infections
- Because irregular bleeding/spotting is common during the first months of Mirena, Kyleena, or Skyla use, exclude endometrial pathology (polyps or cancer) prior to the insertion in patients with persistent or uncharacteristic bleeding
- Follow the insertion instructions exactly as described to ensure proper placement and avoid premature release of the Bayer IUD from the inserter. **Once released, the Bayer IUD cannot be re-loaded**.
- Check expiration date prior to initiating insertion
- Bayer IUDs should be inserted by a trained physician or healthcare provider. They should become thoroughly familiar with the insertion instructions before attempting insertion.
- Insertion may be associated with some pain and/or bleeding or vasovagal reactions (for example, syncope, bradycardia) or seizure in an epileptic patient, especially in patients with a predisposition to these conditions. Consider administering analgesics prior to insertion

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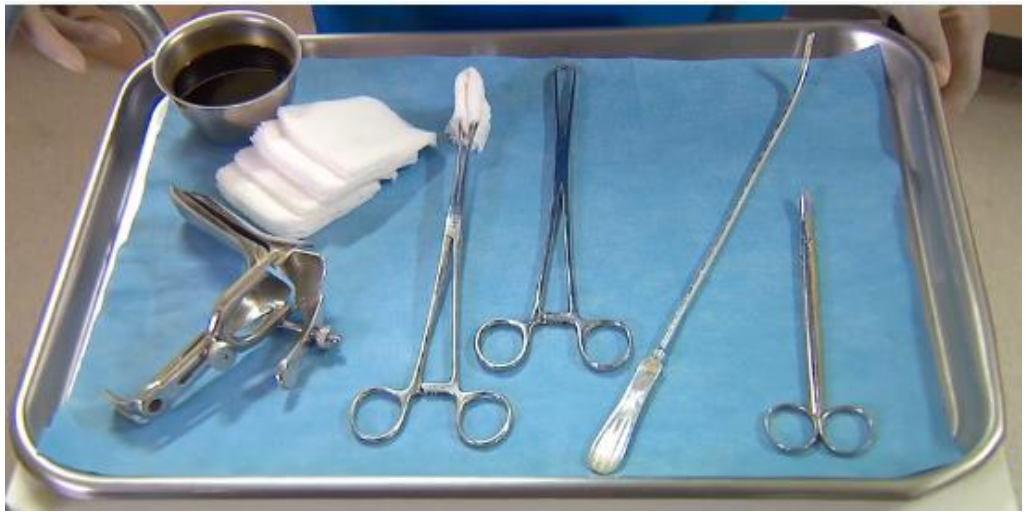
Tools for Insertion

NOTE: The inserter provided with Mirena, Kyleena, and Skyla and the insertion procedure described in this section are not applicable for immediate insertion after childbirth or second-trimester abortion or miscarriage. For immediate insertion, remove the IUD from the inserter (by loading and then releasing it from the inserter), and insert according to accepted practice.

Preparation:

- Gloves
- Speculum
- Sterile Uterine Sound
- Sterile Tenaculum
- Antiseptic solution, applicator



Procedure:

- Sterile gloves
- The prescribed Bayer LNG-IUS with inserter in sealed package (consider having an unopened backup available)
- Instruments and anesthesia for paracervical block, (if anticipated)
- Sterile, sharp curved scissors

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Preparation for Insertion

- Exclude pregnancy and confirm that there are no other contraindications to use of Mirena, Kyleena, or Skyla

- With the patient comfortably in lithotomy position, do a bimanual exam to establish the size, shape and position of the uterus

- Gently insert a speculum to visualize the cervix
- Thoroughly cleanse the cervix and vagina with a suitable antiseptic solution

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Preparation for Insertion

Prepare to Sound the Uterine Cavity

- Grasp the upper lip of the cervix with a tenaculum forceps and gently apply traction to stabilize and align the cervical canal with the uterine cavity
- Perform a paracervical block if needed. If the uterus is retroverted, it may be more appropriate to grasp the lower lip of the cervix
- The tenaculum should remain in position and gentle traction on the cervix should be maintained throughout the insertion procedure

Gentle traction to stabilize and align cervical canal with uterine cavity

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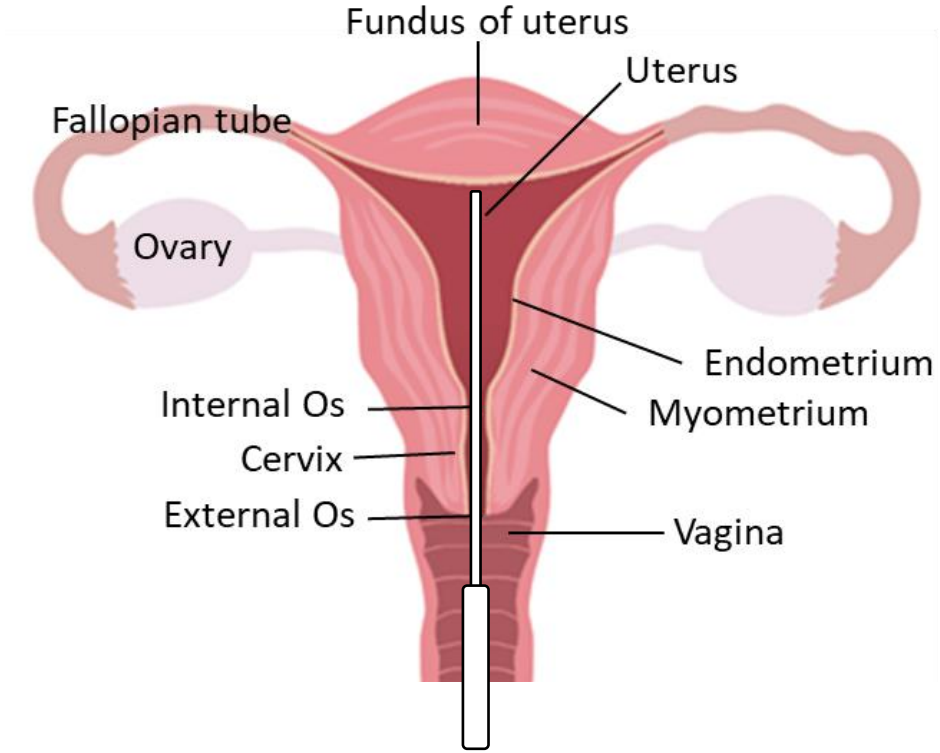
Preparation for Insertion: Sounding

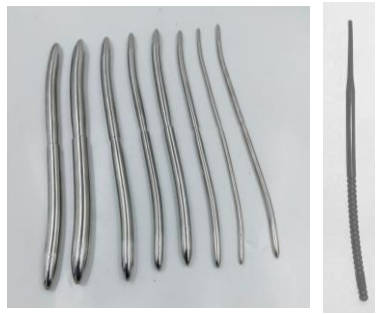


While maintaining traction on the tenaculum, gently insert a uterine sound to:

- check the patency of the cervix,
- measure the depth of the uterine cavity (in cm),
- confirm cavity direction, and
- detect the presence of any uterine anomaly

If you encounter difficulty or cervical stenosis, use dilatation, and not force, to overcome resistance.

- If cervical dilation is required, consider using a paracervical block



Cervical Dilators

All patients should be sounded prior to insertion:

- Patients receiving Mirena should sound between 6-10cm;
- Kyleena and Sykla do not contain a sounding depth requirement

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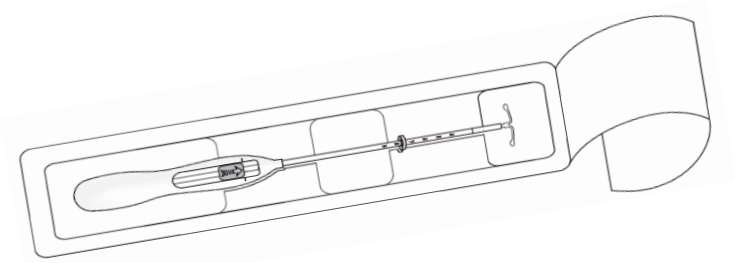
Insertion Steps

Step1 | Step 2 | Step 3 | Step 4 | Step 5 | Step 6 | Step 7 | Cut Threads

Step 1: Open the Package

- The contents of the package are sterile
- Using sterile gloves lift the handle of the sterile inserter and remove from the sterile package



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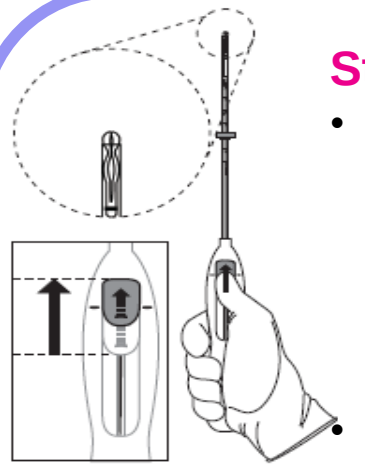
Insertion Steps

Step1 | **Step 2** | Step 3 | Step 4 | Step 5 | Step 6 | Step 7 | Cut Threads

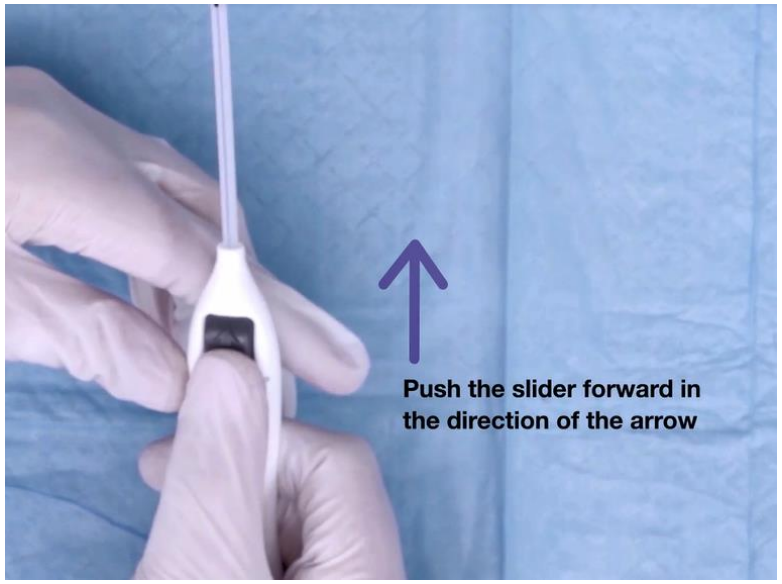


Step 2: Load the IUD into the insertion tube

- Push the slider **forward** as far as possible in the direction of the arrow thereby moving the insertion tube over the T-body to load the IUD into the insertion tube. The tips of the arms will meet to form a rounded end that extends slightly beyond the insertion tube.
- Maintain forward pressure with thumb or forefinger on the slider.

IMPORTANT

DO NOT move the slider downward at this time as this may prematurely release the threads of the IUD. Once the slider is moved below the mark, the IUD cannot be reloaded.



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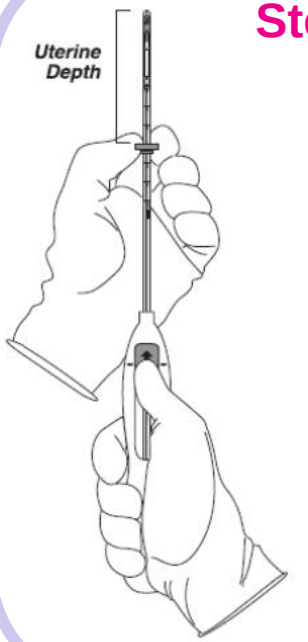
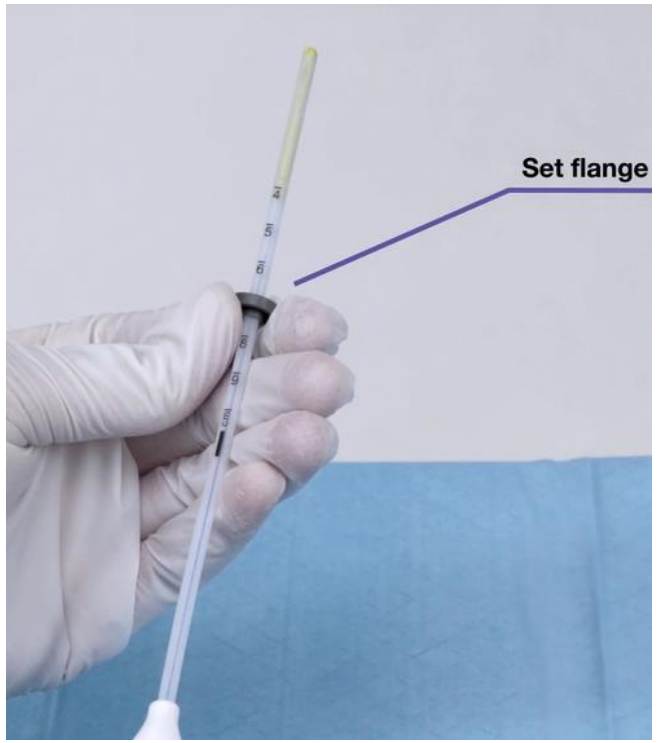


Step 3: Set the Flange

- Holding the slider in this forward position, set the upper edge of the flange to correspond to the uterine depth (in centimeters) measured during sounding**.**

- **For Mirena, the uterus should sound to a depth of 6-10cm.**
- **The Kyleena and Skyla labels do not specify a range for sounding depth**



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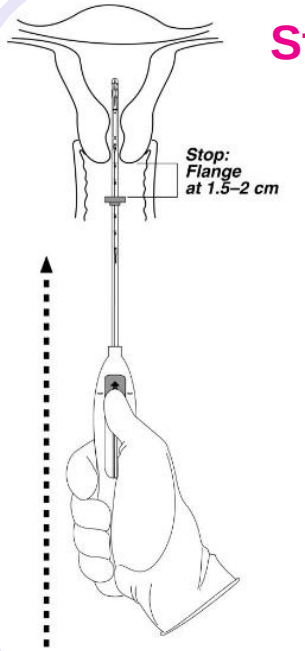
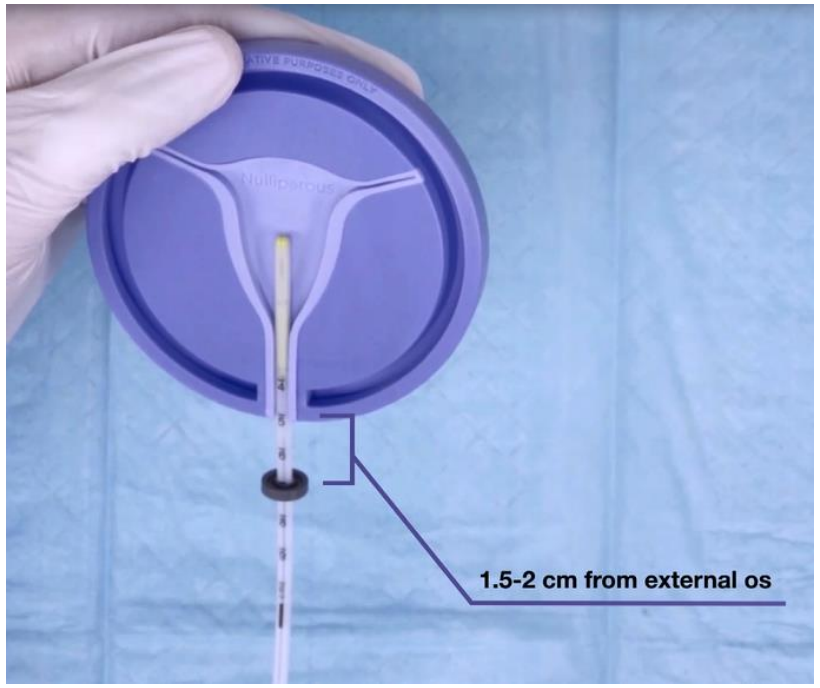


Step 4. The IUD is ready for insertion

- Continue holding the slider in this forward position. Advance the inserter through the cervix until the flange is approximately 1.5 to 2 cm from the cervix and then pause.
- **Do not force the inserter. If necessary, dilate the cervical canal.**



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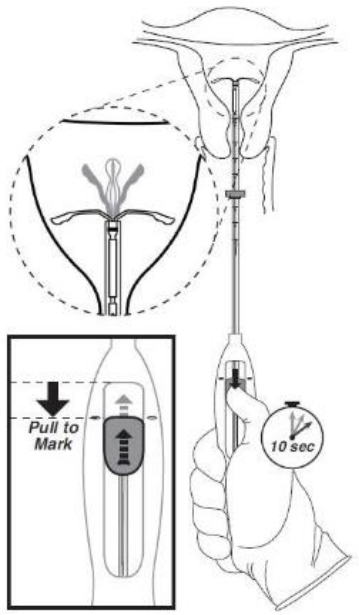
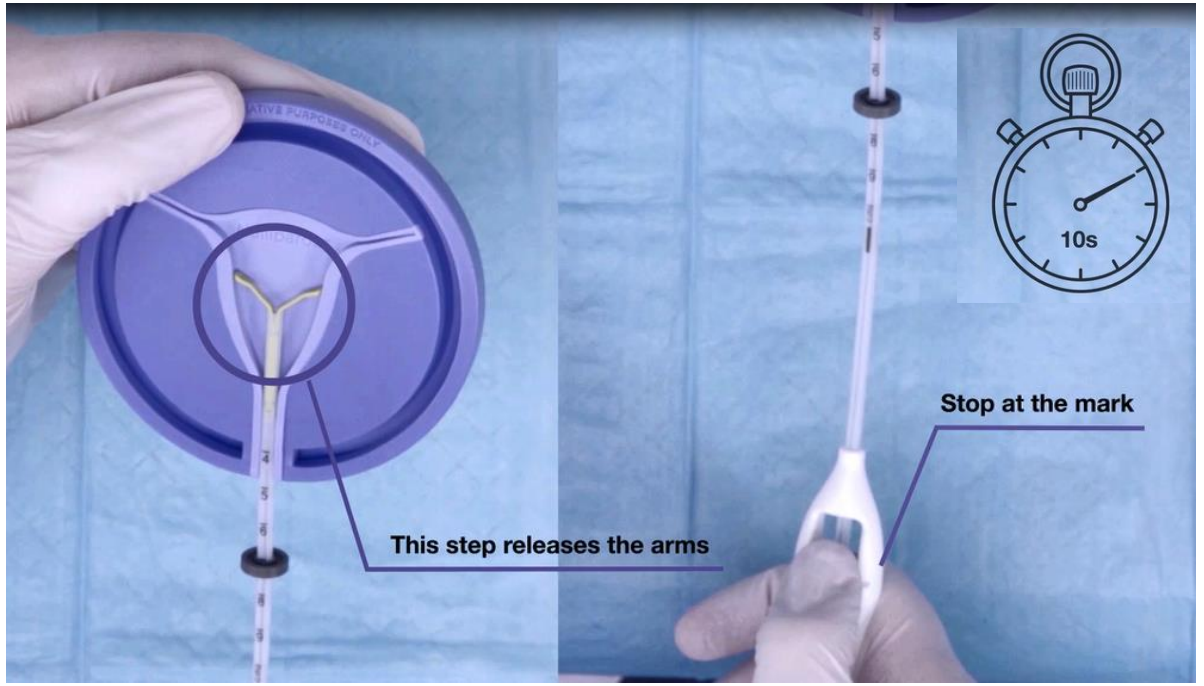
Insertion Steps

Step1 | Step 2 | Step 3 | Step 4 | **Step 5** | Step 6 | Step 7 | Cut Threads

Step 5: Open the arms



- While holding the inserter steady, **move the slider down to the mark** to release the arms of the IUD
- Wait 10 seconds for the horizontal arms to open completely.



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Insertion Steps

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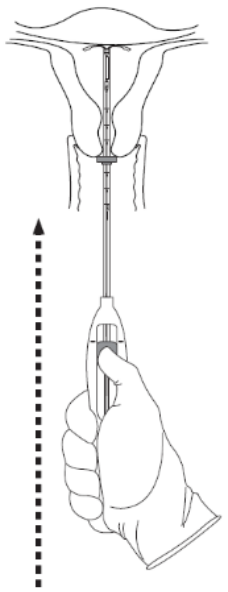
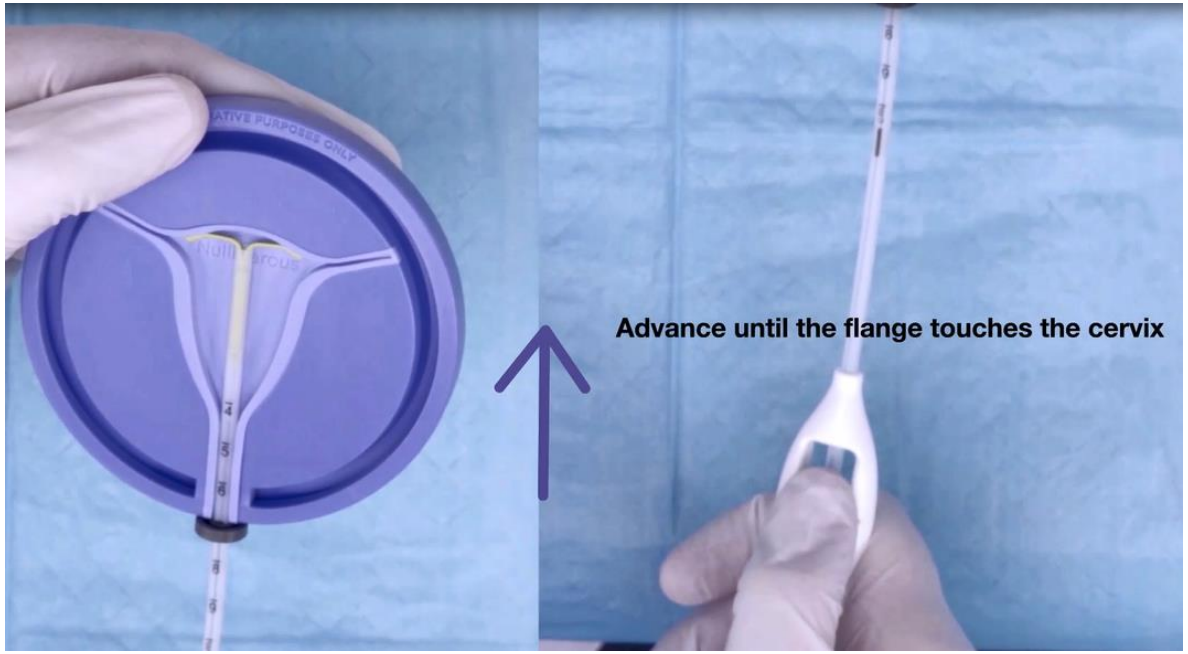
Step 6. Advance to fundal position



- Advance the inserter gently towards the fundus of the uterus **until the flange touches the cervix.**
- If you encounter fundal resistance do not continue to advance.
- The IUD is now in the fundal position.
- **Fundal positioning of Mirena, Kyleena, or Skyla is important to prevent expulsion**



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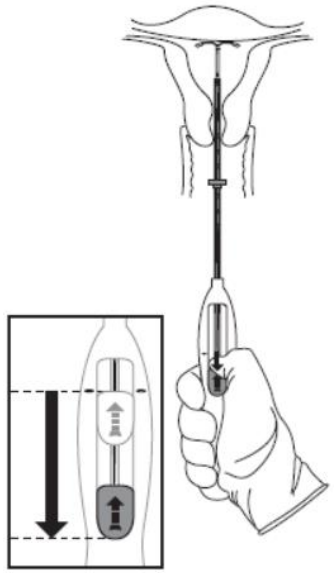
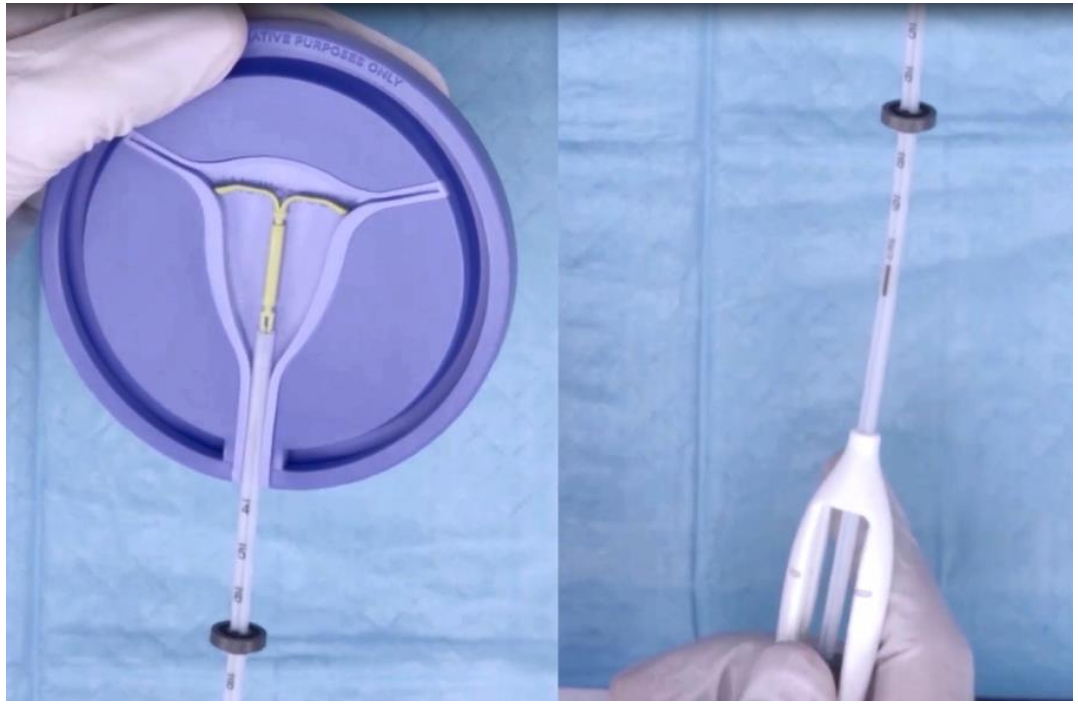


Step 7: Release the IUD and withdraw the Inserter

Holding the entire inserter in place, release the IUD by moving **the slider all the way down.**

Continue to hold the slider all the way down while you slowly and gently withdraw the inserter from the uterus



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Insertion Steps

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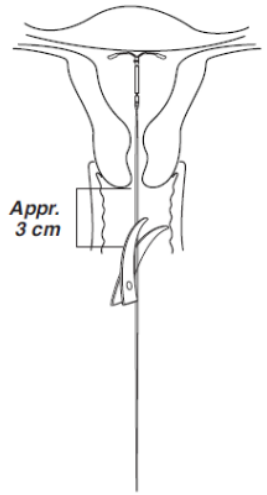
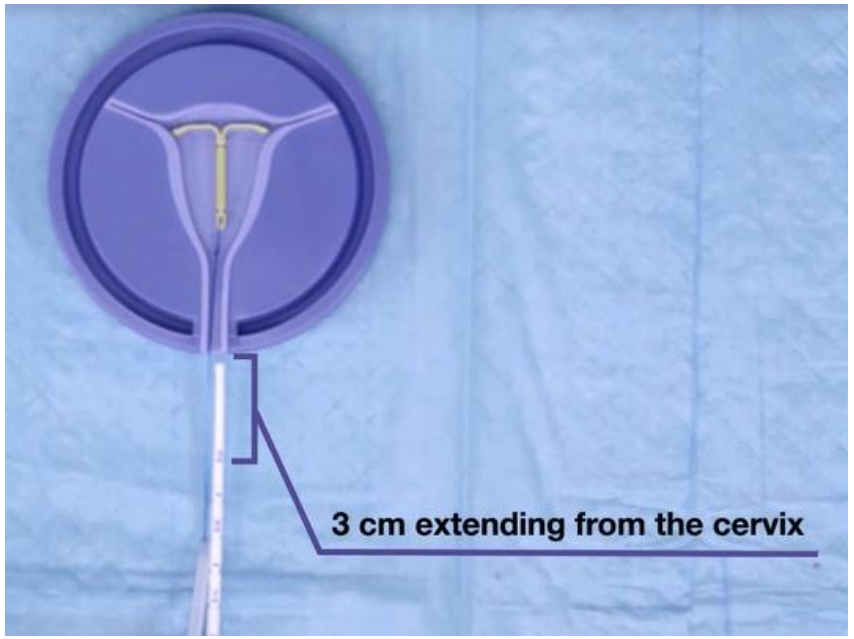
Cut the Threads



Using a sharp, curved scissor, cut the threads perpendicular, leaving about 3 cm visible outside the cervix (cutting threads at an angle may leave sharp ends).

Do not apply tension or pull on the threads when cutting to prevent displacing the IUD

Insertion is now complete. Prescribe analgesics if indicated, and record the lot number in the patient's records



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Insertion Using a Uterine Disc

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Insertion Using a Pelvic Model

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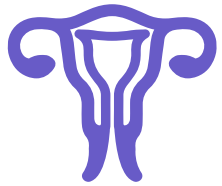
Important Information to Consider During and After Insertion



If you suspect that either Mirena, Kyleena, or Skyla is not in the correct position, check for placement (for example with transvaginal ultrasound)

- Remove a Mirena, Kyleena, or Skyla if it is not positioned completely within the uterus
- Do not reinsert a removed IUD

If there is clinical concern, exceptional pain, or bleeding during or after insertion, appropriate steps (such as physical examination and ultrasound) should be taken immediately to exclude perforation

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Patient Follow-up

Reexamine and evaluate patients **4 to 6 weeks after insertion** and once a year thereafter, or more frequently if clinically indicated

Advise patients to check that their IUD is in place **once a month** by feeling for the threads

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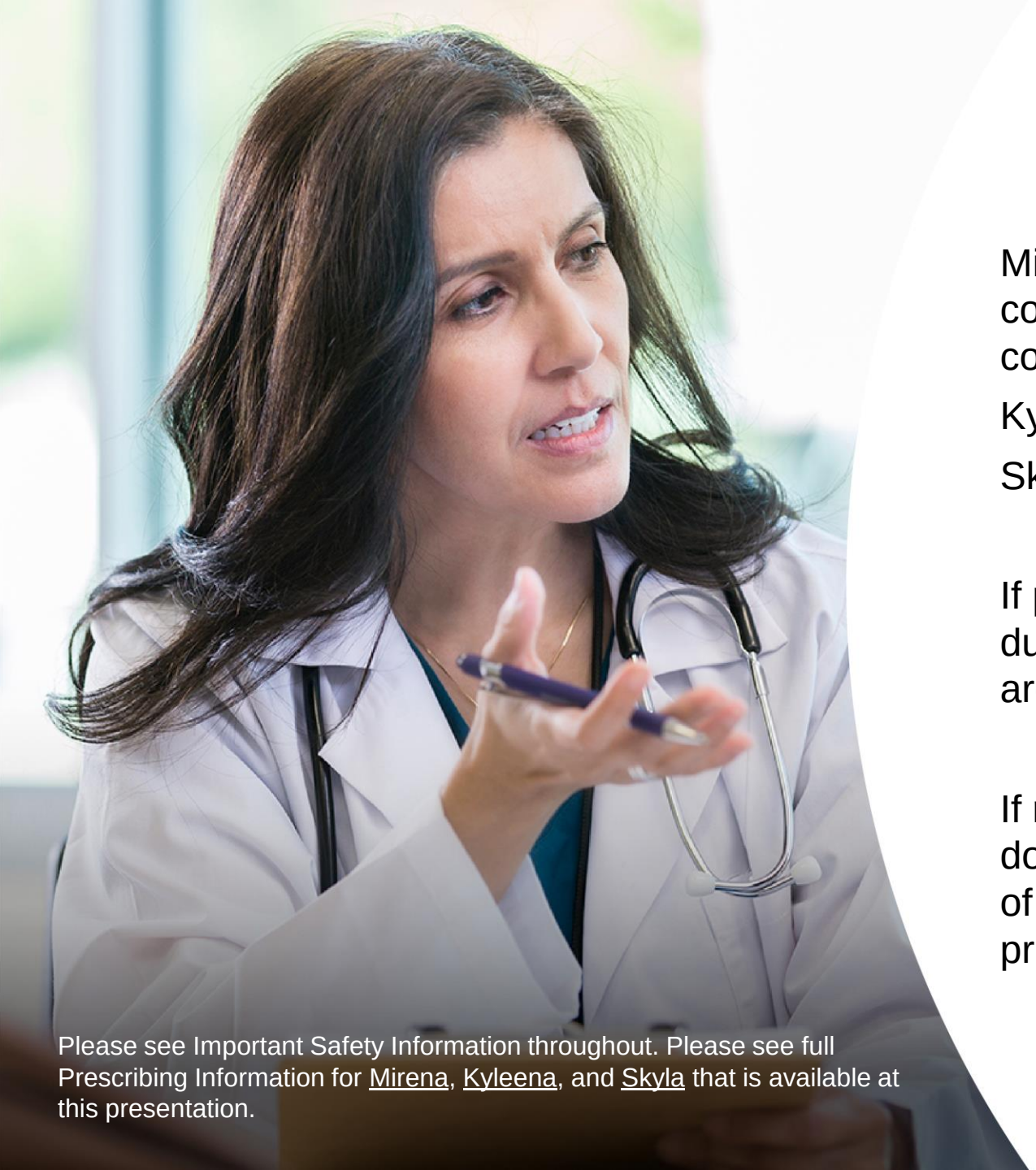

Timing of Removal

Mirena should not remain in the uterus after 8 years for contraception, replace Mirena by the end of 5 years if continued treatment of HMB is needed;

Kyleena should not remain in the uterus after 5 years.

Skyla should not remain in the uterus after 3 years

If pregnancy is not desired, removal should be carried out during the first seven days of menstruation, provided they are experiencing regular menses

If removal will occur at other times during the cycle, or they do not experience regular menstrual cycles, they are at risk of pregnancy: start a new contraceptive method a week prior to removal for these patients

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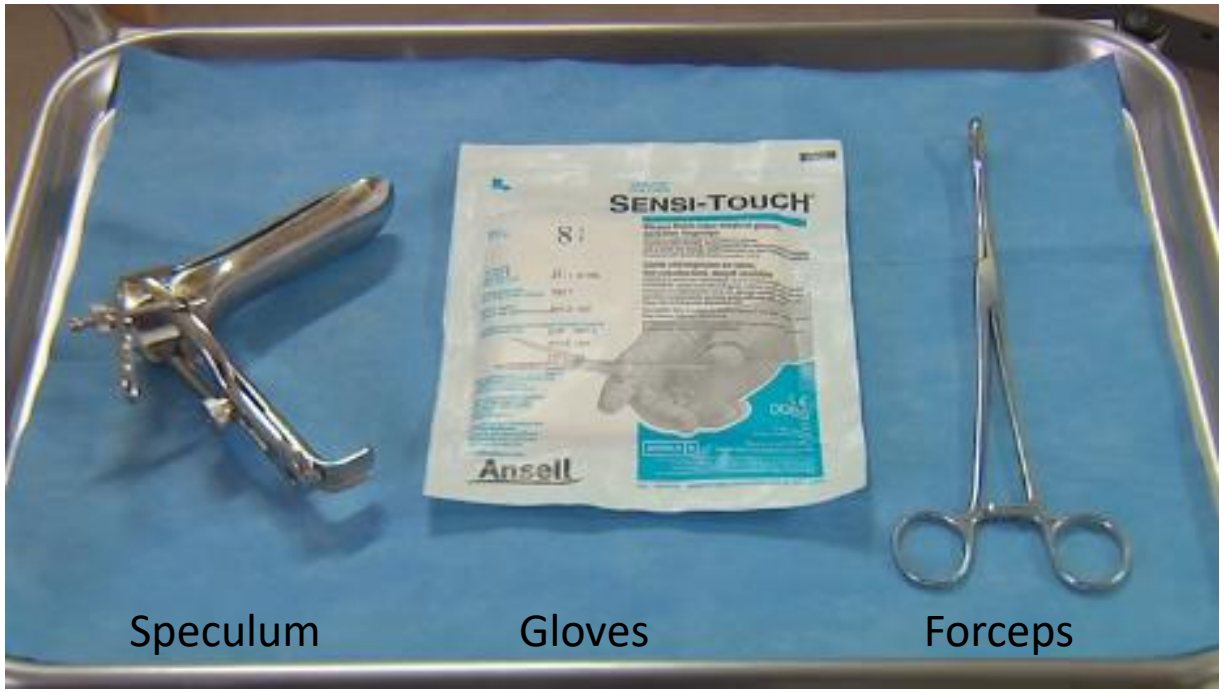
Removal: Tools



Tools for Removal:

- Preparation: gloves, speculum;
- Procedure: sterile forceps

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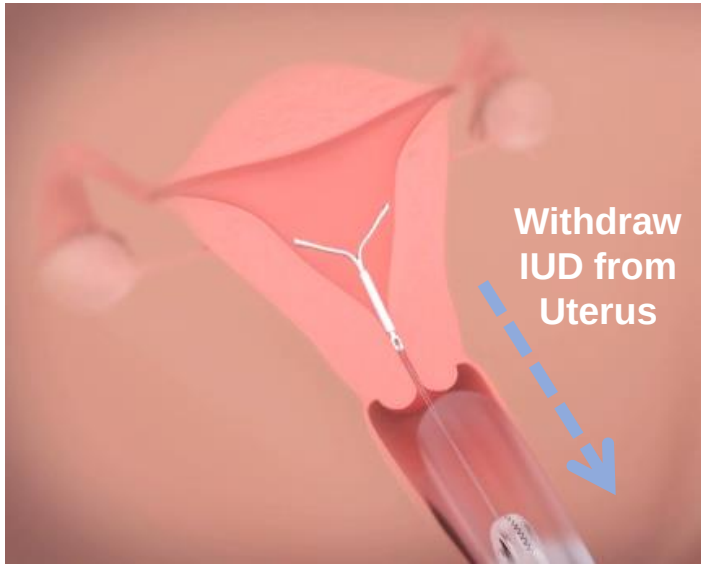
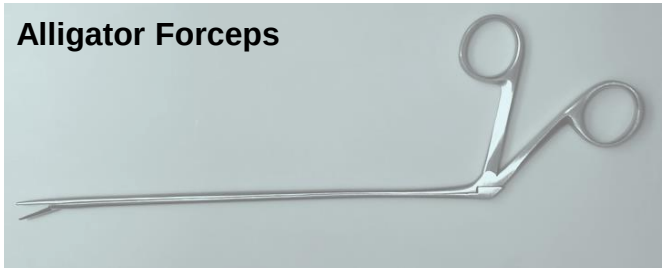
Removal: Procedure



- Remove the IUD by applying gentle traction on the threads with forceps
- If the threads are not visible:
  - Determine location by ultrasound
  - If found to be in the uterine cavity on ultrasound exam, it may be removed using a narrow forceps, such as an alligator forceps. This may require dilation of the cervical canal.



  - After removal, the system should be examined to ensure that it is intact
  - The hormone cylinder of Mirena may slide over and cover the horizontal arms, giving the appearance of missing arms – this generally does not require further intervention once the system is verified to be intact
- If unable to remove with gentle traction, determine the location and exclude perforation by ultrasound or other imaging
- Removal may be associated with:
  - pain and/or bleeding or vasovagal reactions (for example, syncope, bradycardia) or with seizure, especially in patients with a predisposition to these conditions
  - Breakage or embedment in the myometrium can make removal difficult. Analgesia, paracervical analgesia, cervical dilatation, alligator forceps or other grasping instrument, or hysteroscopy may be used to assist in removal

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Continuation of Contraception after Removal

- If pregnancy is not desired and if a patient wishes to continue using Mirena, Kyleena, or Skyla a new system can be inserted immediately after removal any time during the cycle
- If a patient with regular cycles wants to start a different birth control method, time removal and initiation of new method to ensure continuous contraception:
  - Either remove the IUD during the first 7 days of the menstrual cycle and start the new method immediately thereafter, or
  - Start the new method at least 7 days prior to removal if occurring at other times during the cycle
- If a patient with irregular cycles or amenorrhea wants to start a different birth control method, start the new method at least 7 days before removal

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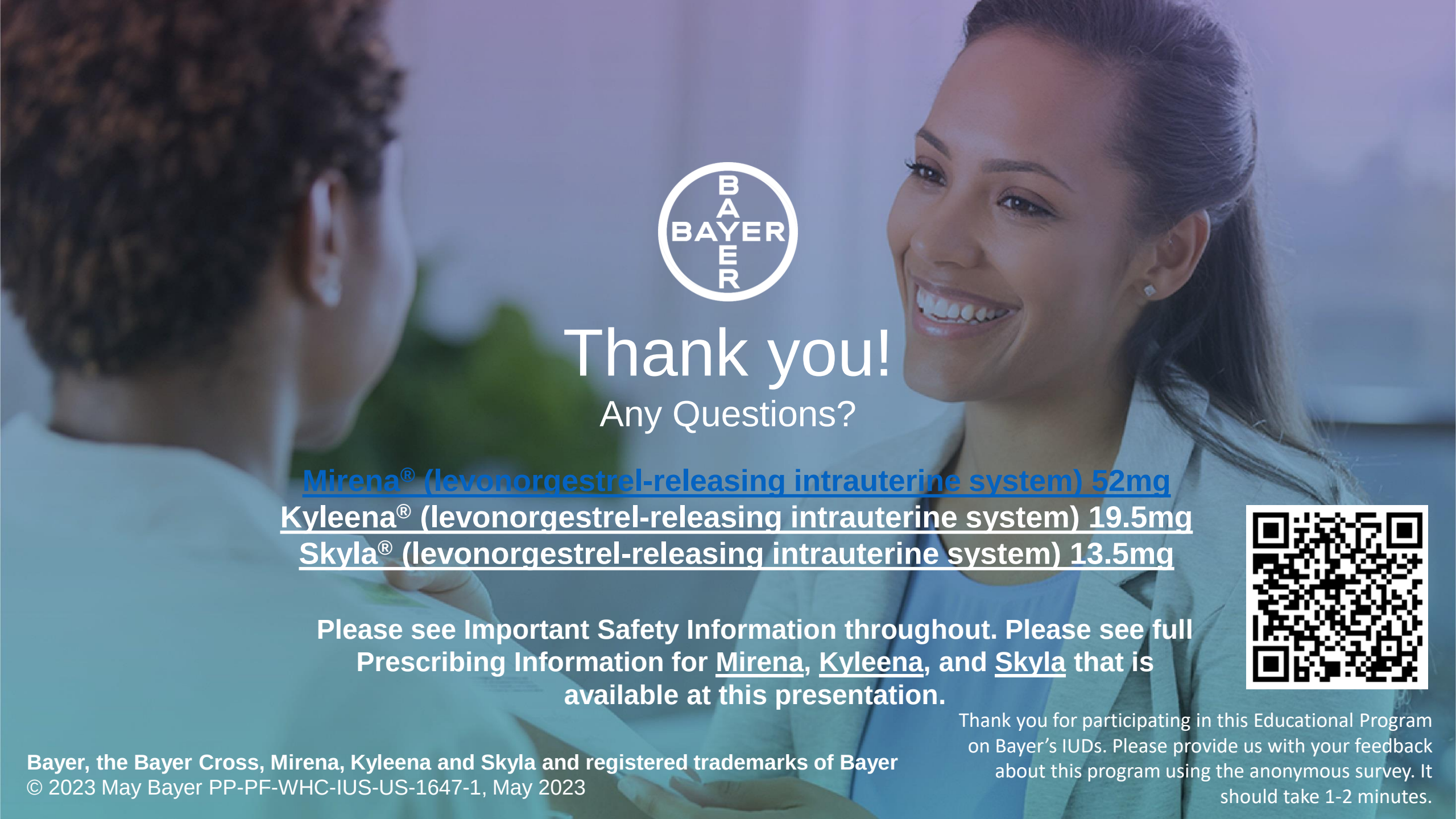

Thank you!

Any Questions?

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Thank you for participating in this Educational Program on Bayer's IUDs. Please provide us with your feedback about this program using the anonymous survey. It should take 1-2 minutes.

Appendix:
Bleeding Patterns

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Mirena

5-Year Contraception Trial (n=1,169 women):

- **~20%** of women developed amenorrhea by the end of the first year

Extension Trial (separate study of n=362 women who used Mirena for more than 5 years):

By the end of 8 years of use:

- **34%** of women experienced amenorrhea
- **26%** experienced infrequent bleeding
- **10%** experienced irregular bleeding
- **3%** experienced frequent bleeding
- **3%** experienced prolonged bleeding

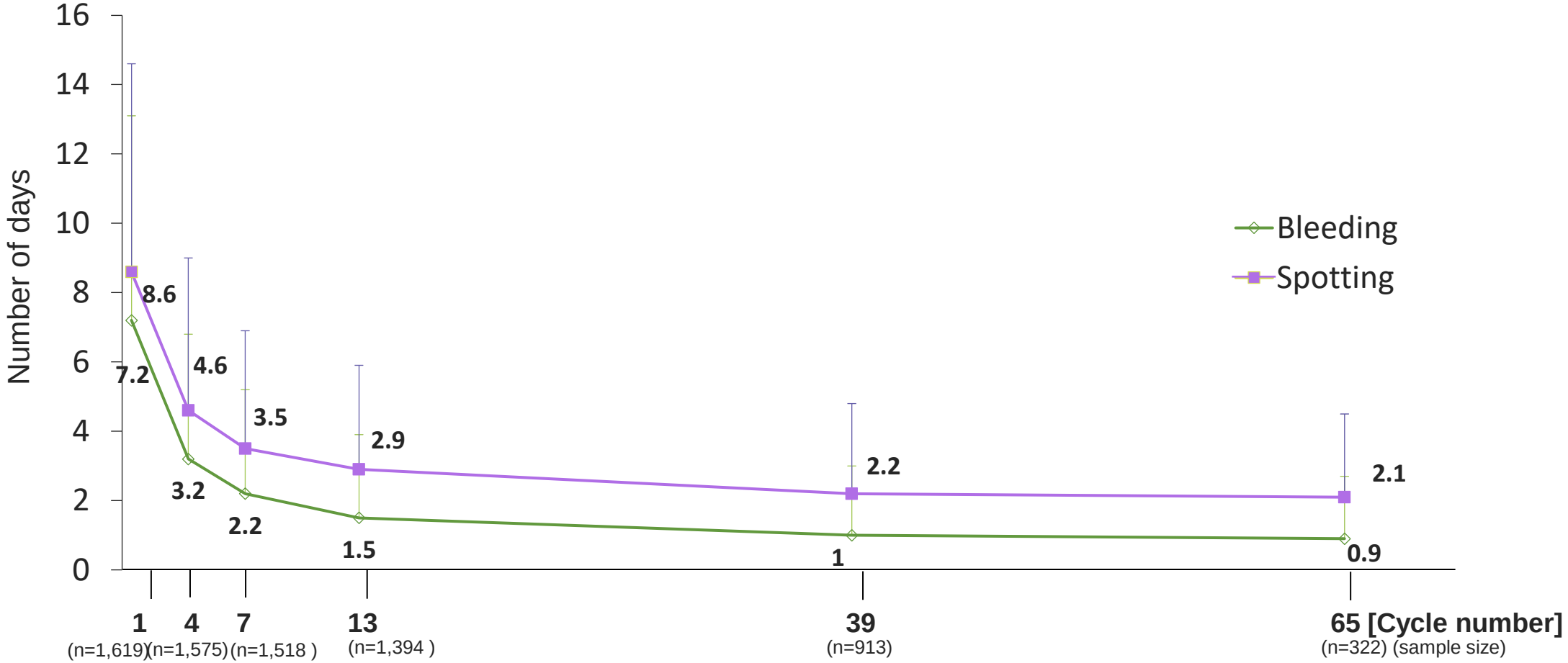
Heavy Menstrual Bleeding Patterns:

- Mirena should be replaced at the end of the fifth year if continued treatment of heavy menstrual bleeding is needed, because data on use in this indication beyond 5 years are limited
- In most women with HMB, the number of bleeding and spotting days may also increase during the initial months of therapy but usually decrease with continued use. The volume of blood loss per cycle progressively becomes reduced

Return to AEs

Kyleena

Mean Number of Bleeding and Spotting-Only Days (28 day cycle equivalent)



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Kyleena

Bleeding Pattern Alterations reported in Contraception Studies (by 90 day reference periods)

Kyleena	First 90 days (n=1,566)	Second 90 days (n=1,511)	End of year 1 (n=1,371)	End of year 3 (n=975)	End of year 5 (n=530)
Amenorrhea (subject with no bleeding/spotting throughout 90 day reference period)	<1%	5%	12%	20%	23%
Infrequent bleeding (subjects with 1 or 2 bleeding/spotting episodes in 90 day reference period)	10%	20%	26%	26%	26%
Frequent bleeding (subjects with > 5 bleeding/spotting episodes in 90 day reference period)	25%	10%	4%	2%	2%
Prolonged bleeding (subjects with bleeding/spotting episodes lasting more than 14 days in the 90 day reference period; may also be included in other category, excluding amenorrhea)	57%	14%	6%	2%	1%
Irregular Bleeding (subjects with 3-5 bleeding/spotting episodes and less than 3 bleeding/spotting free intervals of 14 or more days)	43%	25%	17%	10%	9%

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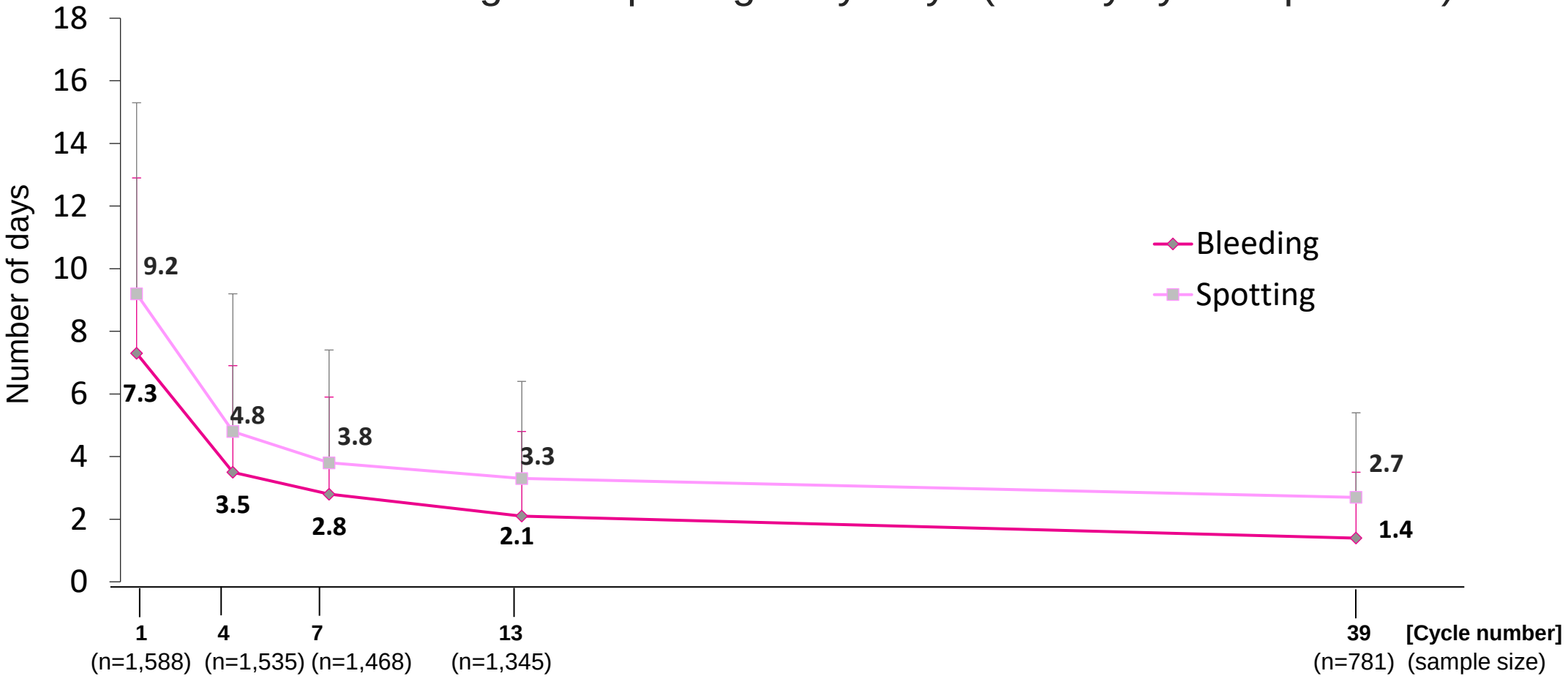
Skyla

Mean Number of Bleeding and Spotting-Only Days (28 day cycle equivalent)



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Skyla

Bleeding Pattern Alterations reported in Contraception Studies (by 90 day reference periods)

Skyla	First 90 days (n=1,531)	Second 90 days (n=1,475)	End of year 1 (n=1,329)	End of year 3 (n=903)
Amenorrhea (subjects with no bleeding/spotting throughout 90 day reference period)	<1%	3%	6%	12%
Infrequent bleeding (subjects with 1 or 2 bleeding/spotting episodes in 90 day reference period)	8%	19%	20%	22%
Frequent bleeding (subjects with > 5 bleeding/spotting episodes in 90 day reference period)	31%	12%	8%	4%
Prolonged bleeding (subjects with bleeding/spotting episodes lasting more than 14 days in the 90 day reference period; may also be included in one of the other categories -excluding amenorrhea)	55%	14%	6%	2%
Irregular Bleeding (subjects with 3-5 bleeding/spotting episodes and less than 3 bleeding/spotting free intervals of 14 or more days)	39%	25%	18%	15%

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