

Contraception Update 2019

September 10th 2019

Minnesota Reproductive and
Sexual Health Update

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envisionsrh.com



This presentation includes discussion of use of products “off-label”.

When the speaker mentions use of medications for purposes other than what is included in their FDA label they will be identified as such.

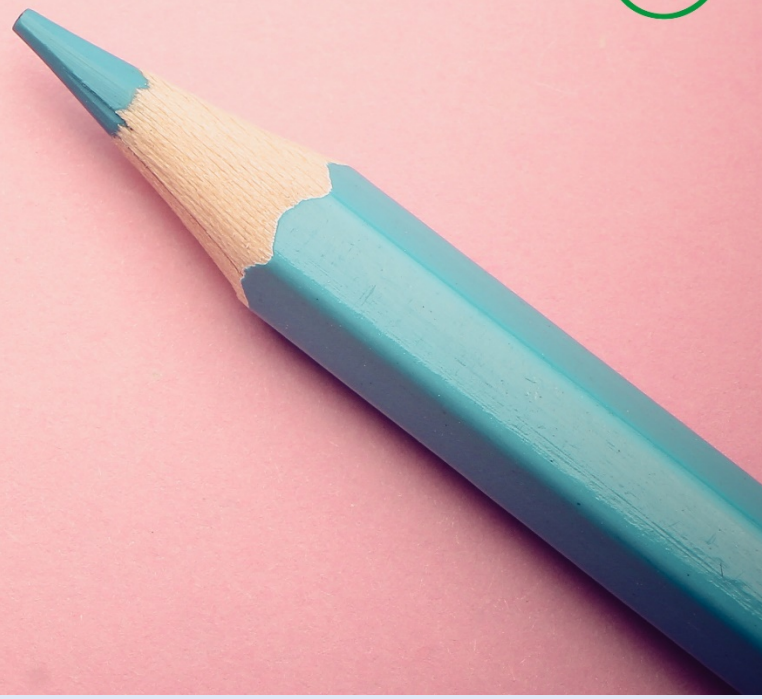
Objectives

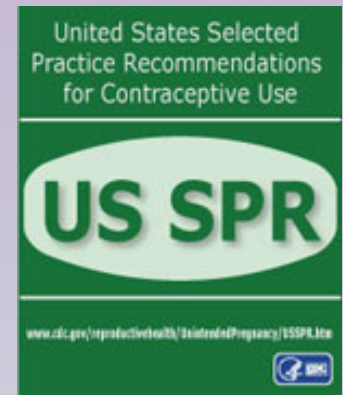
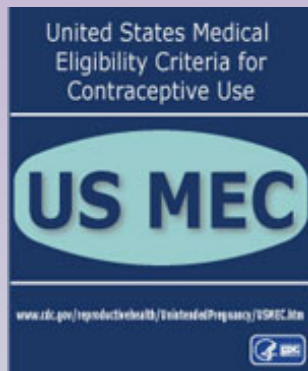
- Describe two innovations in contraception
- Discuss extended use of implants and IUDs
- Demonstrate use of patient-centered questions to assist patients with contraceptive decision making

Outline

- Update on best practices
- New contraceptive products on the market
- Contraceptive products in development

BEST PRACTICE





U.S. Medical Eligibility for Contraceptive Use

U.S. Selected Practice Recommendations

Providing Quality Family Planning Services: Recommendations of the CDC and U.S. OPA

UTILIZE NATIONAL GUIDELINES



Find the APP

- ✓ Play store on android
- ✓ App store on iPhone
 - ✓ Go to search field
 - ✓ Type in: Contraception CDC



US Medical Eligibility Criteria: Categories

1	No restriction for the use of the contraceptive method for a woman with that condition
2	Advantages of using the method generally outweigh the theoretical or proven risks
3	Theoretical or proven risks of the method usually outweigh the advantages – not usually recommended unless more appropriate methods are not available or acceptable
4	Unacceptable health risk if the contraceptive method is used by a woman with that condition

U.S. Selected Practice Recommendations

Provides recommendations on optimal use of contraceptive methods for persons of all ages, including adolescents.



Ask About Reproductive Goals **PATH**

PA: Parenting/Pregnancy Attitudes:

Do you think you might like to have (more) children at some point?

T: Timing: When do you think that might be?

H: How Important: How important is it to you to prevent pregnancy (until then)?

(Hatcher, R.A, et, al. 2018. Geist, C., et, al. 2019. Callegari, Aiken et al. 2017)

Reproductive Intention/Goals

Clarifies
motivation
and degree
of
acceptability
regarding
pregnancy

...so we can
offer
appropriate
interventions

+/-
Contraception

+/-
Preconception
Care

Infertility
Services or
Adoption

“Do you have a sense of what is important to you in your birth control method?”

Best Question



Use Visual Aids & Tactile Aids

HOW WELL DOES BIRTH CONTROL WORK?

What is your chance of getting pregnant?



Really, really well



The Implant



Hormonal IUDs



Non-hormonal IUD



Sterilization,
for men and women

Works, hassle-free, for up to...

4 years

3-6 years

12 years

Forever



Less than 1 in 100 women



Pretty well



The Pill



The Patch



The Ring



The Shot

For it to work best, use it...

Every. Single. Day.

Every week

Every month

Every 3 months



6-9 in 100 women,
depending on method



Not as well



Withdrawal



Fertility Awareness



Internal Condom



Condom

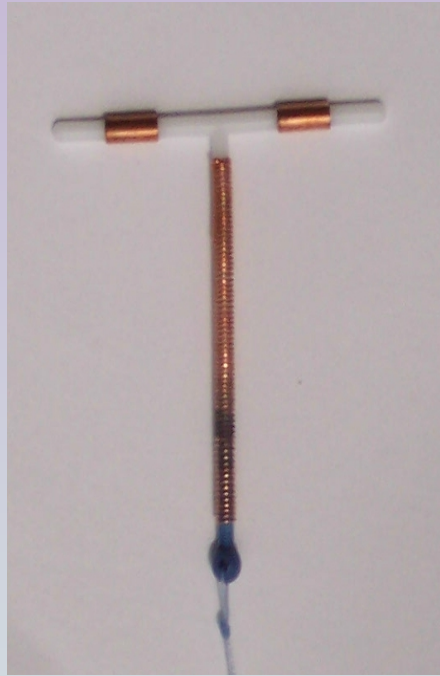
For each of these methods to work, you or your partner have to use it every single time you have sex.

Use a condom with any other method for STI protection.

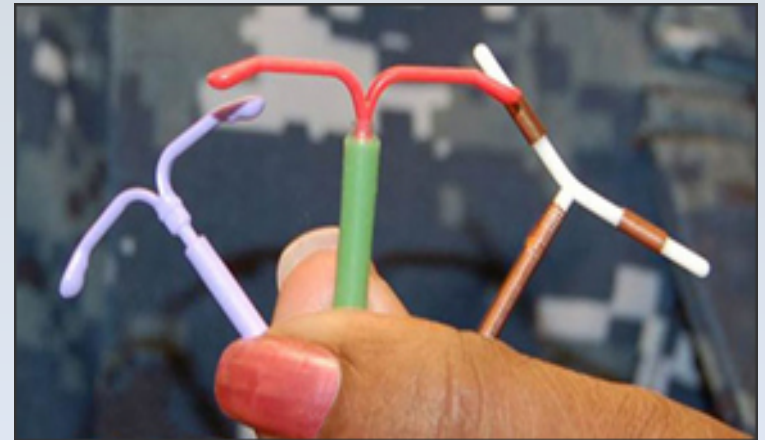
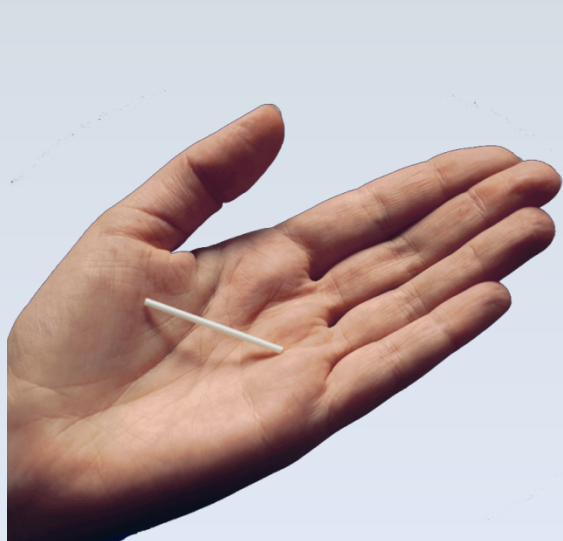


12-24 in 100 women,
depending on method

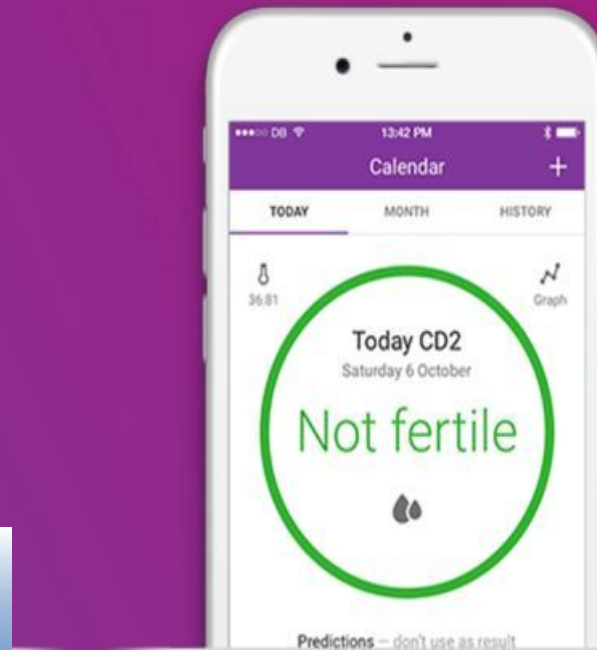
FYI, without birth control,
over 90 in 100 young women
get pregnant in a year.



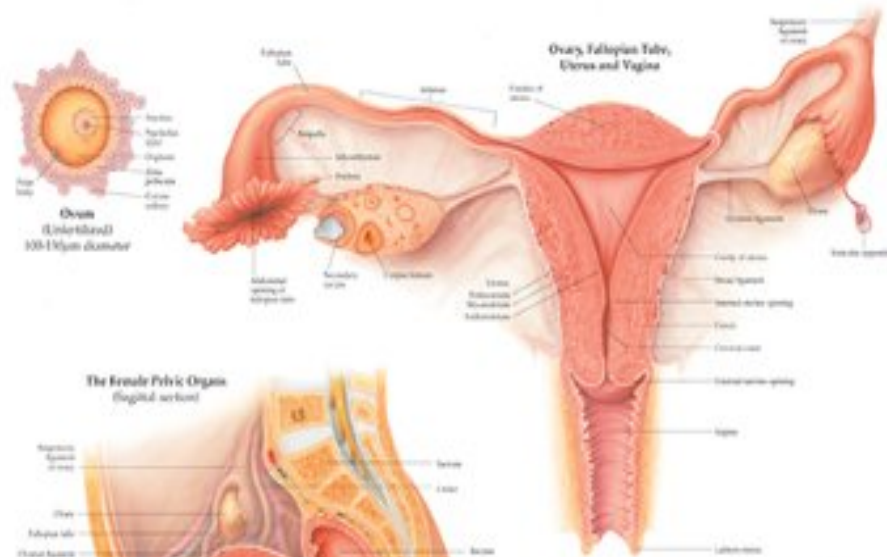
Tactile Aids







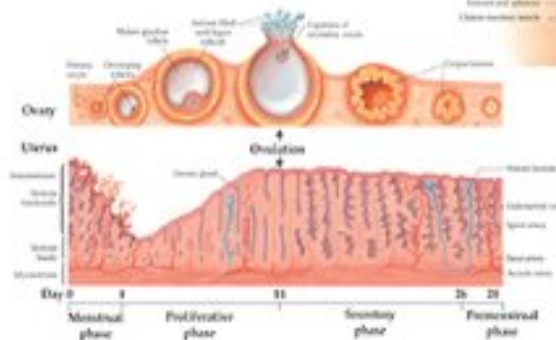
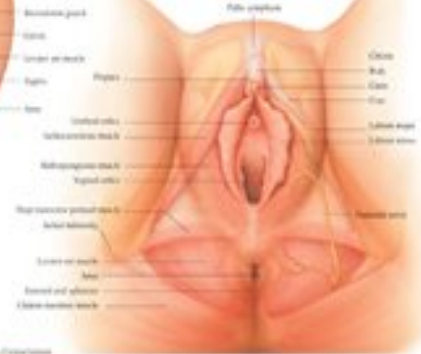
THE FEMALE REPRODUCTIVE SYSTEM



The Female Pelvic Organs
(Sagittal section)



The Female Perineum
(Frontal view)



The Menstrual Cycle

The menstrual cycle is a series of changes in the female reproductive system that occurs in females of reproductive age. The cycle is controlled by the hormones estrogen and progesterone, which are secreted by the ovaries. The cycle is divided into four phases: Menstrual phase, Proliferative phase, Secretory phase, and Premenstrual phase.

Menopause

Menopause is the point in a woman's life when she stops having menstrual periods. It is a natural part of aging and is usually accompanied by a variety of symptoms, including hot flashes, night sweats, and changes in the menstrual cycle.

THE MALE REPRODUCTIVE SYSTEM



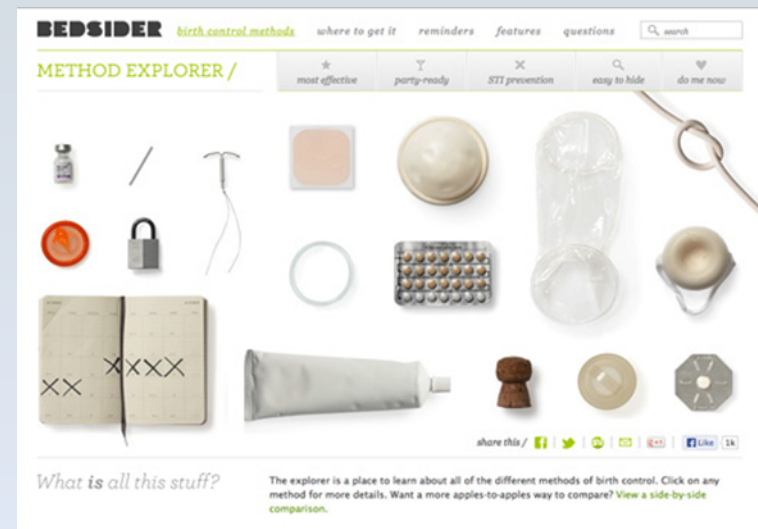
BEDSIDER--Patient Education Resource



*Give your patients birth
control materials they'll love.*

[Http://bedsider.org/](http://bedsider.org/)

- “User friendly”, **accurate** information on all contraceptive methods
- Will set up reminders for contraception adherence and appointments
- Patient testimonials
- Free provider resources



Bedsider.org is ALSO a Provider Resource

[Http://bedsider.org/](http://bedsider.org/)

Find:

- How to prevent a vasovagal
- A patient testimonial about vasectomy
- Posters for the office

Prevent Vasovagal Reactions



Pre-syncopal Signs + Symptoms

- Facial pallor (distinct green hue)
- Diaphoresis, feeling warm or cold
- Sudden need to go to the bathroom
- Nausea
- Yawning
- Pupillary dilatation
- Weakness, light-headedness
- Visual blurring/ tunnel vision



STOP Vasovagal Syncope

- Isometric contractions of the extremities
- Intense gripping of the arm, hand, leg and foot muscles
- No need to bring the legs together or change position just tense the muscles



Vasovagal Prevention

- Anticipatory guidance!
- Good hydration
- Eat before placement
- Prophylactically contract muscles if known history



(Grubb 2005)

Non-delayed Contraception



- Quick start all methods
- Same day placement of implant, and IUDs
 - the patient wants it placed that day
 - no contraindications

Dispense More Pills, Patches, & Rings

Provision of 13 cycles

- Halves pregnancy and abortion rates
- Improves continuation of use
- Decreases coverage gaps

Offer Continuous Use Combined Hormonal Contraceptives

- Delays or eliminates bleeding
- More effective; less ovarian activity
- More margin for user error
- Demonstrated safety
- Less PMS/PMDD
- Rx extended-use brand
- Or just skip hormone-free interval



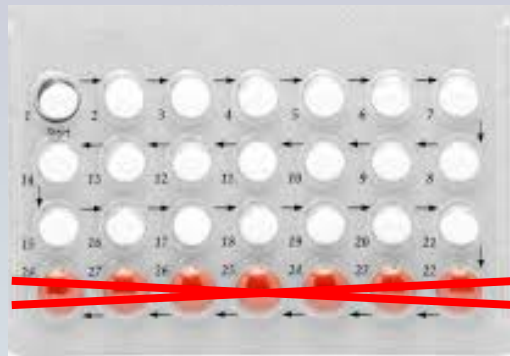
Continuous Use Combined Oral Contraceptives



- Monophasic



- 21 days



- Or 24 days



- Continuous use means NO PLACEBO, no hormone-free interval (HFI)

Continuous Use Vaginal Ring

- Goal is no bleeding
- Ring left in place in vagina for 1 month
- First day of each calendar month switch ring!
- Each ring has enough hormone to last at least 6 weeks
- 4 day HFI when needed

Depo Medroxyprogesterone Acetate (DMPA, “the shot”, Depo-Provera)



DMPA Where, When, & How?

- Effective through 15 weeks
- Use a long enough needle
- Do not massage after injection
- DMPA – SQ 104 mg/0.65mL

DMPA & Fracture Risk

- DMPA use was associated with slightly increased fracture risk compared with other methods
- The absolute risk of fracture was small
- No increased risk of fracture was observed after discontinuation
- Use of DMPA beyond 2 years should not be considered an absolute contraindication

DMPA and Weight Gain

- DMPA users who gain $\geq 5\%$ of their baseline weight within 6 months are predicted to continue gaining... and gaining
- We can use this information to counsel those at risk of excessive weight gain

(Bonny, Secic et al. 2011; dos Santos Pde, Modesto et al. 2014; Le, Rahman et al. 2009; Lopez, Ramesh et al. 2016; Pantoja, Medeiros et al. 2010; Risser, Gedter et al. 1999)

DMPA and Metabolism

- Changes occur in carbohydrate metabolism in DMPA users
- Decrease in lean body mass
- Increase in % body fat
- Data show regular aerobic exercise may exert a protective effect

*DMPA Return to Fertility **Precaution***

- May not return to ovulation, menstruation or fertility for > 1 year
- Delay in return to fertility can occur regardless of the length of use

**IN CASE OF
EMERGENCY**



Tiers of Emergency Contraceptive (EC) Effectiveness

1. Top tier: Copper IUD (Paragard)
2. Second tier: Ulipristal acetate (UPA) (ella)
3. Third tier: Levonorgestrel (LNG) (Plan B)



- Effectiveness of oral EC decreases with increasing weight
- Majority of pregnancies occur **subsequent to EC use** due to continued unprotected sex

Quickstarting Hormonal Contraception After UPA

*“After using ella, if a woman wishes to use **hormonal contraception**, she should do so **no sooner than 5 days after the intake of ella**, and she should use a reliable barrier method until the next menstrual period.”*

Patient asks for EC



Counsel for use of copper IUD



What is her BMI?

<25

26-29

30-34

≥35

Oral EC
options
acceptable

Counsel
that **LNG**
likely
ineffective

Oral EC
failure rate
4x higher.
LNG
ineffective

Counsel
that **UPA**
likely
ineffective

Cu IUD for EC

- Failure rate ZERO-0.09%.
- Provides ongoing contraception
- High continuation rates
- New data showing **no pregnancies** when placed 6-14 days after unprotected sex with a negative pregnancy test



Thompson, I. et, al. 2019
Cleland K et al. 2012
Wu S, et al. 2010
Turok et al. 2013.

REMOVAL



Expectation Among Providers About Duration Of Use

Unlike with other reversible contraceptives

- high up-front cost,
- the focus on continuation rates in some studies
- the fact that most common side effects are short lived
- the name “long-acting” reversible contraception

Amico, J. R., (2017)

Amico, J. R., (2016)

If you would like it out for any reason...

- Reframe the concept of “early” removal
- No particular duration of use of an implant or an IUD is expected

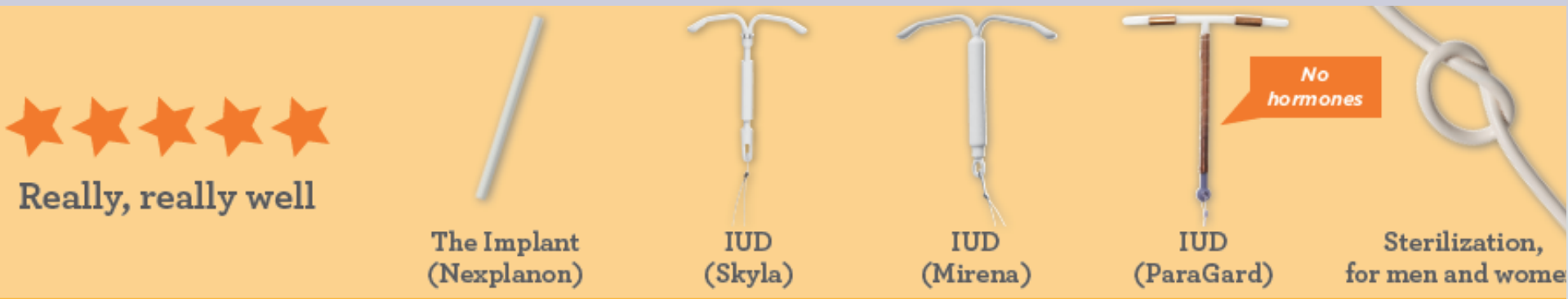
Language for LARC

“This method is good for **up to** ____ years but if you want to get pregnant before then or you would like it out for any reason, come in, we will remove it and your ability to get pregnant will go back to whatever is normal for you immediately.”



WHAT'S NEW

TOP TIER



<1% failure

Nexplanon® Procedure-related Events

7364 procedures

- Incorrect placement 1%
- Pins and needles/numbness in the arm/hand/fingers was the most common patient-reported event
- The most common challenge reported by HCPs during placement was removal of the end cap

Nexplanon® Procedure-related Events

7364 procedures

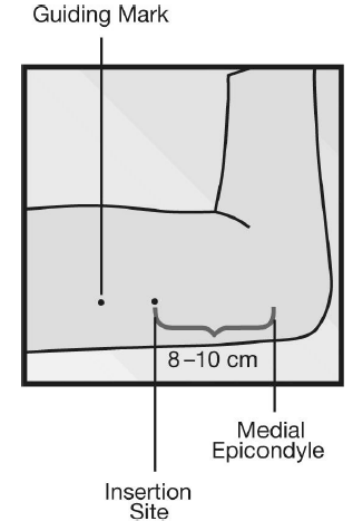
- No implants were localized outside the arm
- The most common challenge reported by HCPs during removal was fibrotic tissue

Migration of Implant

1.3 Migrations per Million Placements

N=38 cases of migration:

- lung/pulmonary artery (n=9)
- chest wall (n=1)
- vasculature at locations other than the lung/pulmonary artery (n=14)
- extravascular migrations (n=14) to other body sites (e.g., the axilla and clavicle/neck line/shoulder)



New Location and Arm Position

- No major neurovascular structures were identified overlying the triceps:
 - 8–10 cm proximal to the medial epicondyle
 - and 3–5 cm posterior to the sulcus
- Elbow flexion deflects the ulnar nerve away from this area and may further decrease risk of injury

Clinicians are now advised
to avoid placement in the biceps groove,
no matter how superficial that placement
might be

Place
over the
triceps



Is the Implant Effective in Obese People?

- Package insert states:

“No Studies in women >130% of their ideal body weight”

- Highly effective, including among people with high BMI

Lazorwitz, A. et. Al. 2019 Lopez, Bernholc et al. 2016;
Mornar, Chan et al. 2012; Morrell, Cremers et al.
2016; Xu, Wade et al. 2012

Menstrual Effects: Cu IUD

NSAIDs prophylactically with food

- **Pre-emptive use for first 3 cycles**
- Start before onset of menses-- anti-prostaglandin effect
 - Naproxen sodium 220mg x2 BID (max 1100mg/day)
 - Ibuprofen 600-800mg TID (max 2400mg/day)



Comparing bleeding patterns for the levonorgestrel (LNG) 52 mg, 19.5 mg, and 13.5 mg intrauterine systems (IUS)

Amenorrhea after the first 6 months:

- LNG 52mg (11%)
- LNG 19.5mg (5%)
- LNG 13.5mg (3%)

Bleeding patterns for the LNG 52 mg, LNG 19.5 mg, and LNG 13.5 mg IUS

Infrequent bleeding (after 1 year):

- LNG 52 mg (31%)
- LNG 19.5 mg (26%)
- LNG 13.5 mg (20%)

Irregular Bleeding After 90 days

- LNG 52 mg (6%)
- LNG 19.5 mg (17%)
- LNG 13.5 mg (23%)

Frequent & Prolonged Bleeding

- Similar over 2 years for all products
- LNG 13.5 mg more frequent or prolonged bleeding than LNG 19.5 mg and LNG 52 mg

Conclusions

- 52 mg LNG IUS has more amenorrhea and infrequent bleeding than lower doses
- Users of 52 mg LNG IUS have less irregular bleeding than people using IUSs with lower doses



Implant

LNG 52 IUD

EXTENDED USE

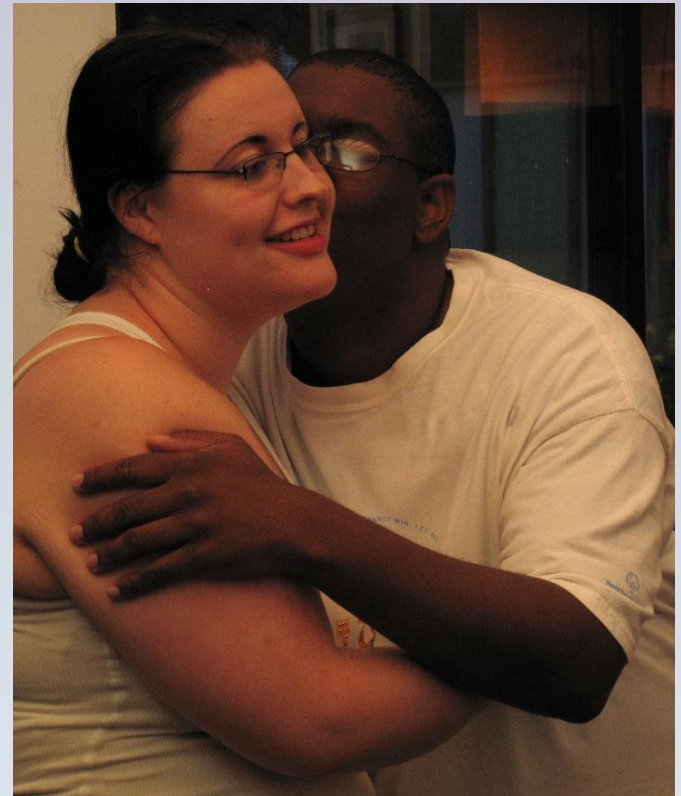
Etonogestrel implant



- The EPIC Study-- part of Contraceptive Choice project, 291 women provided 444 user-years of extended use. No pregnancies.
- 7-country study, 390 used implant beyond 3 years more than 200 of them used for at least 5 years. No pregnancies.

Threshold For Ovulation Suppression >90 pg/mL

Serum ENG median
levels remained above
90 pg/mL for women of
all BMIs



(McNicholas, Swor et al. 2017)

>90 pg/mL



- The absolute threshold of contraceptive effectiveness remains poorly defined
- The threshold of effectiveness may be <90 pg/mL because cervical mucus changes may prevent pregnancy should ovulation occur

Levonorgestrel-releasing Intrauterine System 52 Mg



7 Year Data



- Approved for up to 5 years
- Data show that it is highly effective for at least 2 additional years of use
- 6th year failure rate 0.25
- 7th year failure rate 0.43 (n=496)
- Another trial showed 7-year pregnancy cumulative failure rate 0.5 (n=398)

52-mg LNG-IUD Data Suggest



- Efficacy as long as 15 years
- HCPs & policy makers could take advantage of the present information to decide to maintain the same device at *least up to seven years*
- Furthermore, amenorrhea could be a good indicator of contraceptive effect

Liletta* Levonorgestrel-releasing Intrauterine System 52 Mg



*The 340B price
for Liletta is \$50

LNG 52 LILETTA

- FDA approved use up to 5 years
- Submitted to FDA for 6 year indication
- The clinical trial is ongoing to 10 years
- LNG content at 5 year supports equivalence to Mirena and efficacy to at least 7 years



New Products



Second Tier



Pretty well



The Pill



The Patch



The Ring



The Shot

For it to work best, use it...

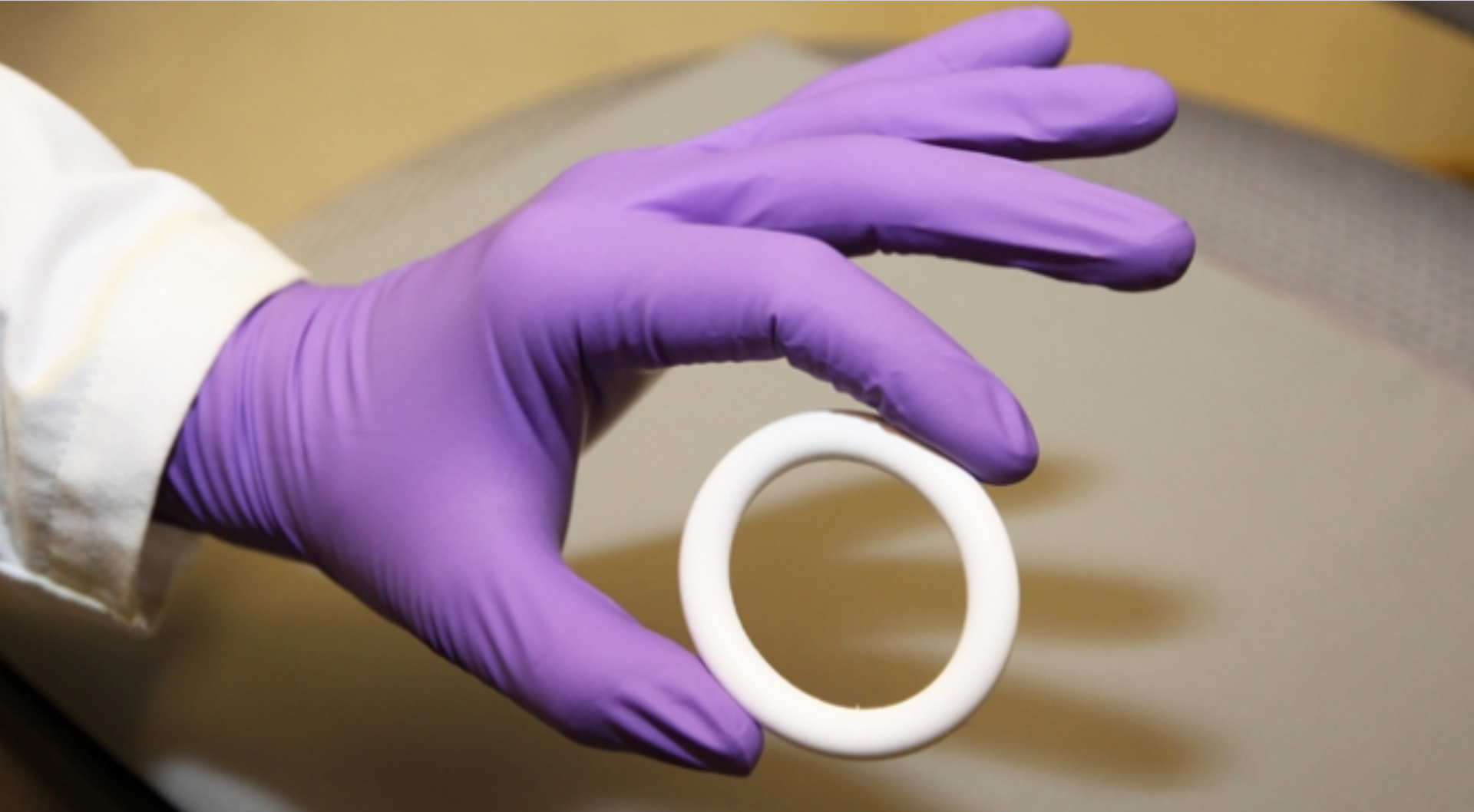
Every. Single. Day.

Every week

Every month

Every 3 months

Annovera Contraceptive Vaginal Ring (CVR)



One-Year Vaginal Contraceptive Ring

- Segesterone acetate (Nestorone[®]) + ethinyl estradiol
- Developed by the Population Council
- Two phase 3 open-label safety & efficacy trials

One-Year Vaginal Contraceptive Ring

- Commercially available Fall 2019! NOW
- Participants ranked high in convenience, ease of use, and satisfaction
- Side effect & bleeding profile similar to NuvaRing
- Does not require refrigeration



Use of the Annovera CVR

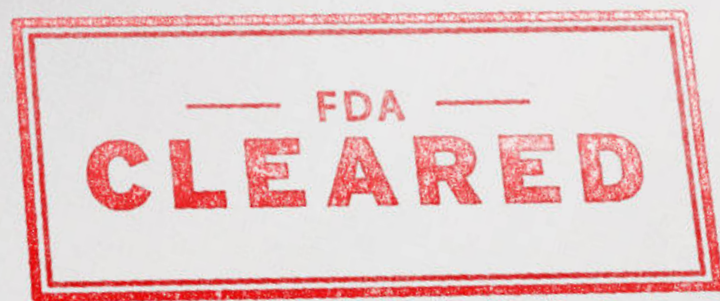
- In for 21 days, then removed for 7 days to induce a scheduled bleed (like a menses)
- Can remove for up to 2 hours for intercourse or cleaning
- Can use water-based creams and lubricants
- Can *not* use oil and silicone-based lubricants as they alter exposure to EE and segesterone acetate

Annovera CVR

- TherapeuticsMD has agreed to provide significantly reduced pricing to Title X family planning clinics
- Not in same FDA contraceptive category as NuvaRing, so *must* be covered under no cost-sharing rules of ACA

Comparison

	NuvaRing	Annovera
Lifespan	6 weeks	1 year (13 cycles)
Progestin release rate	Etonogestrel 120 mcg/day	Nestorone 150 mcg/day
Ethinyl estradiol release rate	15 mcg/day	13 mcg/day
Diameter	54 mm	56 mm
Thickness	4 mm	8.4 mm



Drospirenone (DRSP) 4 mg Progestin-only Pill (POP) Slynd™

- DRSP is progestin in: Yaz, Yazmin, Ocella
- 24/4 Dosing Regimen
 - 24-hour missed pill window
- No estrogen to increase thromboembolic risk
- Commercially available early Fall 2019! NOW

DRSP 4 mg

- Perfect use Pearl index (based on 14,329 cycles) of 0.73 which is equivalent to currently available combined hormonal pills
- No case of deep vein thrombosis or pulmonary embolism

DRSP 4 mg

Laboratory parameters, weight, heart rate, and blood pressure showed no statistically significant changes due to the treatment

DRSP 4 mg

- Diuretic effect like spironolactone; may help PMDD, PCOS, hirsutism
- One case of hyperkalemia
- Slynd™ is contraindicated in people with conditions that predispose to hyperkalemia (e.g. renal impairment, hepatic impairment and adrenal insufficiency)

K⁺

Check serum potassium levels during the first treatment cycle in those receiving daily, long-term treatment for chronic conditions or diseases with medications that may increase serum potassium concentrations.

Best News



No back-up
needed if <24
hours since
missed pill

Because DRSP Has a Long Half Life

- 30-33 hour half life
- The other currently available POP contains northindrone which has a 8-9 hour half life!

Third Tier



Not as well



Withdrawal



Fertility Awareness



Internal Condom



Condom

Use a condom with any other method for STI protection.

For each of these methods to work, you or your partner have to use it every single time you have sex.



12-24 in 100 women,
depending on method



<https://www.myonecondoms.com/>

- **10 lengths. 9 widths. 60 sizes.**
- Standard condoms can sometimes feel too tight, too loose, too short, too long. Sound familiar? That's because most condoms were the same size. Until now.
- You wouldn't settle for one-size-fits-all pants or shoes. Penises come in many different sizes. Isn't it about time condoms did, too?
- Find a condom that's perfectly fit for you.

Female Condom FC2



Internal Condom

- Comes with silicone-based lubricant on the inside
- Additional lubrication can be used
- Does not have to be water soluble
- Does not contain spermicide
- STI protection that doesn't rely on a partner maintaining an erection

Internal

- Helps to prevent pregnancy, STIs & HIV
- Can be used during anal sex (remove the inner ring)
- Now available with a prescription for no cost

Uninsured or Underinsured

- Patient Assistance Program
 - 12-Pack for \$28.95
 - 24-Pack for \$47.95
- 340B Prime Vendor Program (PVP)
 - 12-Packs of FC2

Fertility Awareness Based Methods (FABMs)

Intro to FABMs in NCTCFP webinar:

<https://bit.ly/2LVnrb3>

Two General Categories of Apps

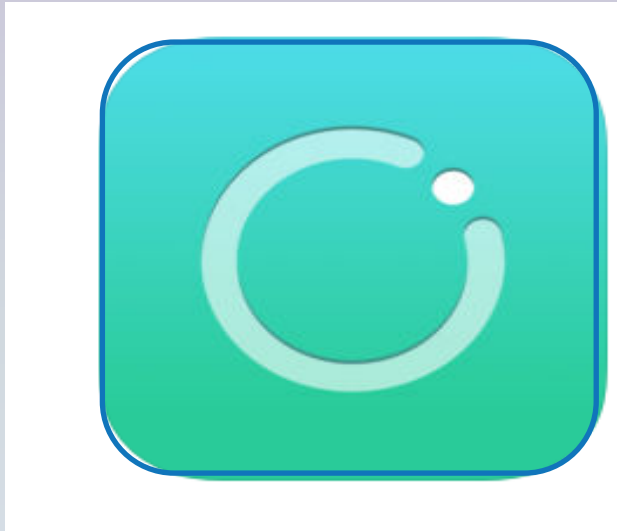


Digital Platforms
For Existing FABMs



Algorithms

Algorithms



Dot algorithm
coming soon



Natural Cycles

11:04 AM 54%

< Search



Natural Cycles - Birth Control

Fertility & Birth Control App

GET

In-App Purchases



4.8 ★★★★★

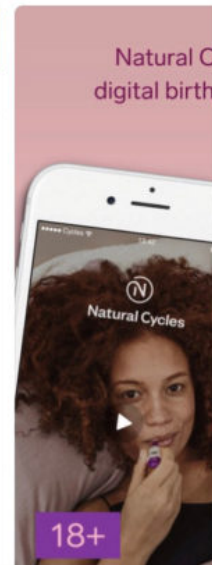
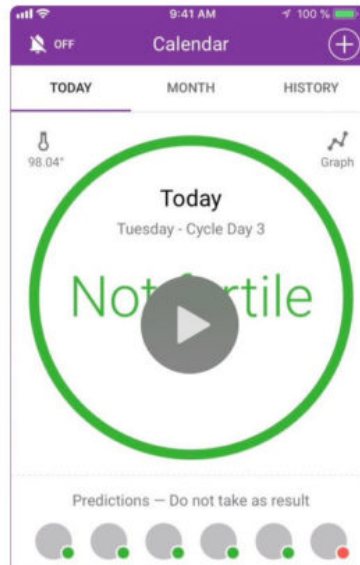
2.59K Ratings

#195

Health & Fitness

17+

Age



Today



Games



Apps



Updates



Search



CONTRACEPTIVE METHODS IN DEVELOPMENT

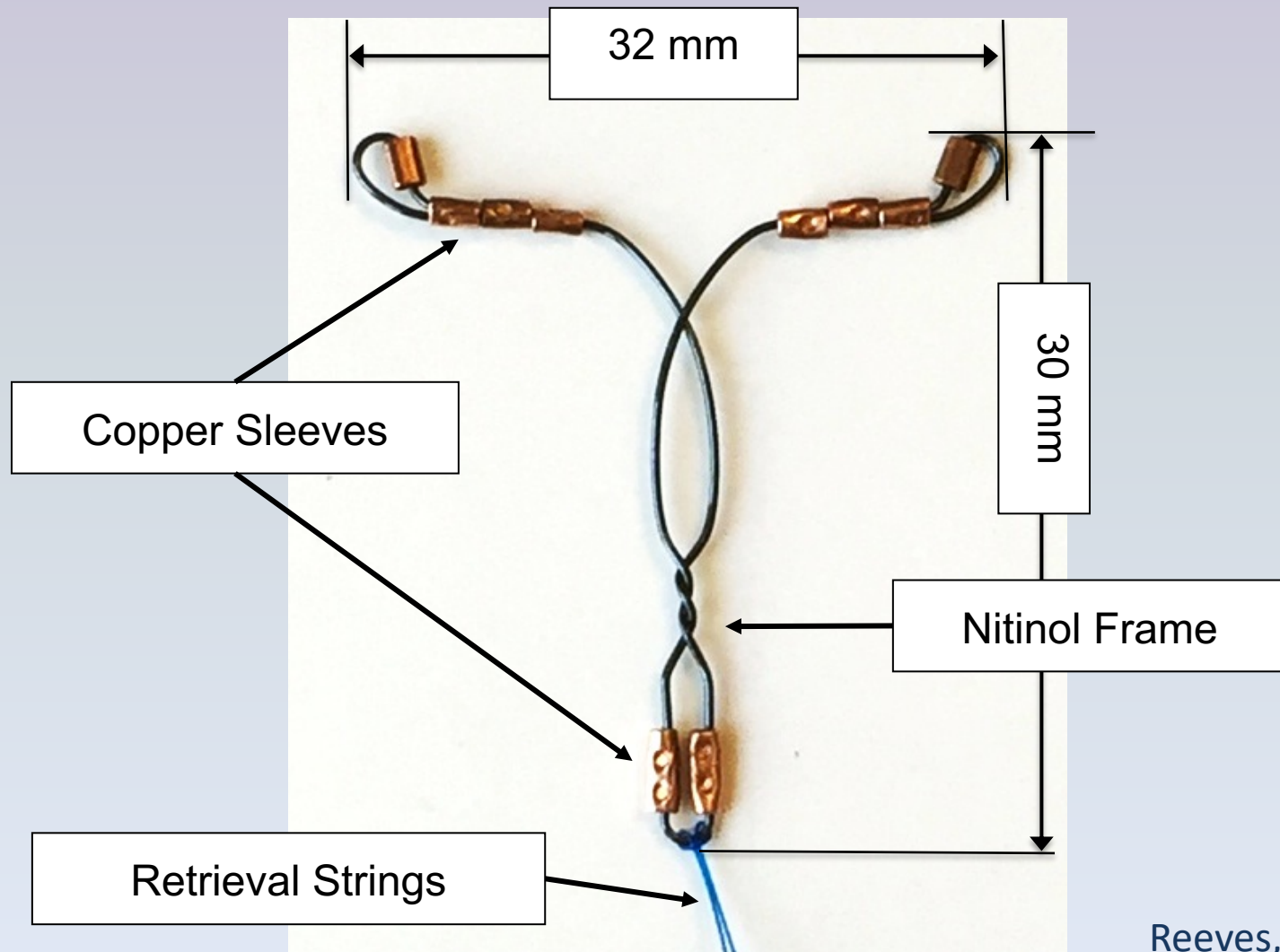
VeraCept

In Phase 3

- 175 mm² of copper
 - Near cervix and cornua
- Nitinol frame
 - Shape memory allows pre-loading
 - Small diameter inserter (3.7mm)
 - Compliant arms
 - Fundus seeking
- Pre-cut strings

VeraCept

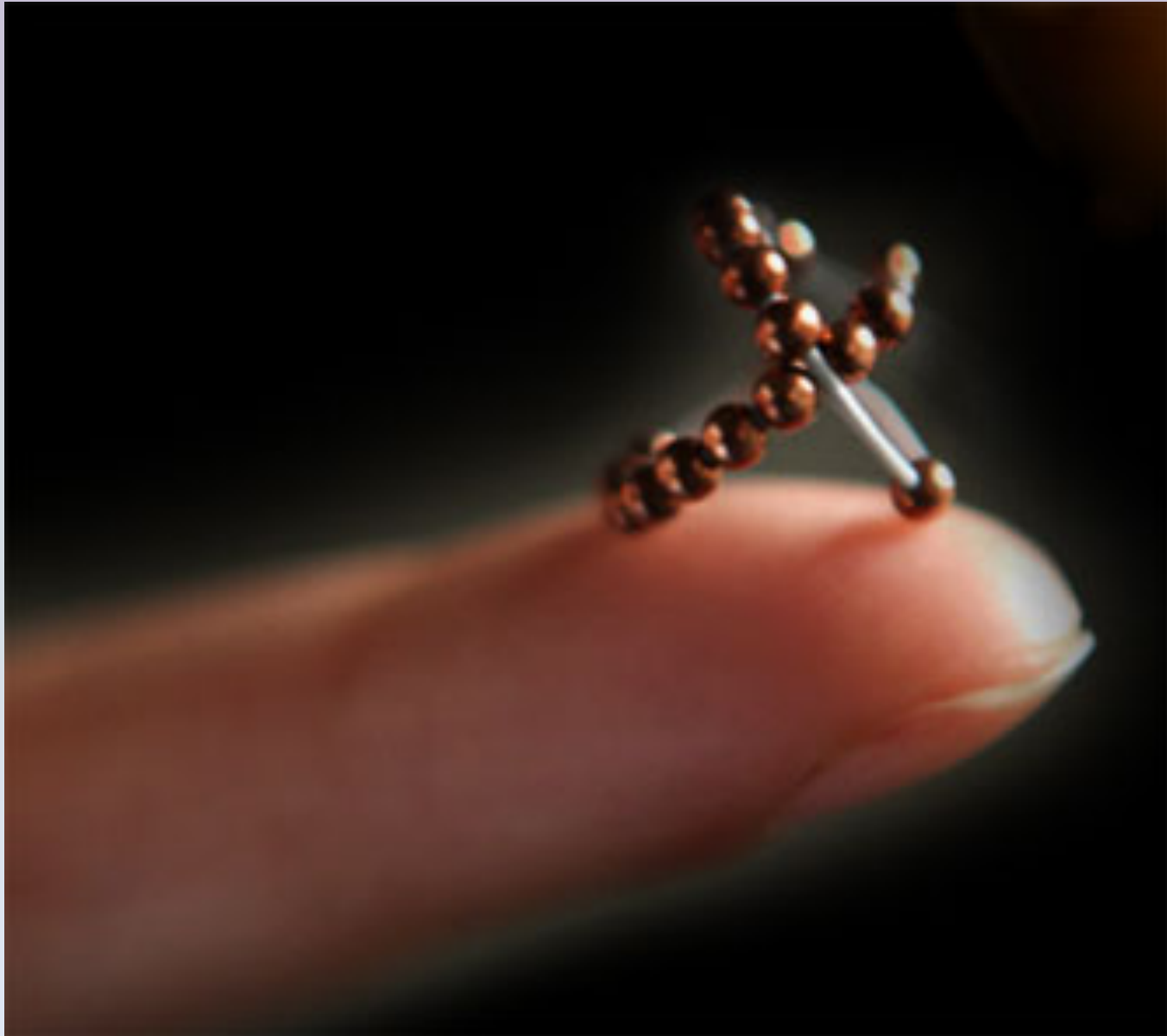
Intrauterine Copper Contraceptive



IUB™

- Spherical intrauterine platform
- Nitinol frame; a biocompatible nickel-titanium alloy (used in vascular stents and Essure)
 - The IUB™ adapts to the uterine cavity
- 3 sizes ranging from 12 mm to 18 mm in diameter
- Out of 49 placements 9 expulsions

IUB™



Head to Head

Comparison with Paragard

- Mona Lisa[®] NT Cu380 Mini
 - Copper surface of 380 mm²
 - 24 mm wide X 30 mm long
- Based on the Nova T 380
- Polyethylene frame with barium sulfate

Mona Lisa[®] NT Cu380 Mini



LevoCept Phase 2

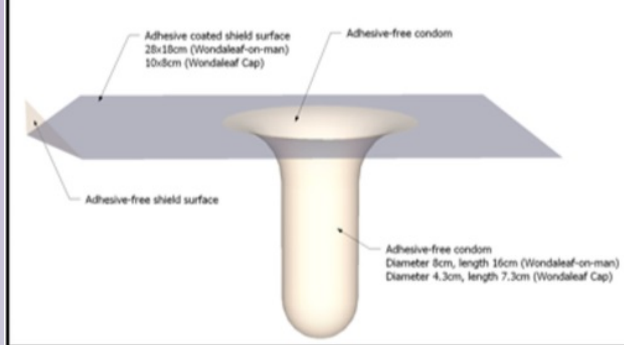
- LNG 52mg on a nitinol frame (like VeraCept)
- Primary outcome measure is effectiveness
- Other outcome measures include
 - Ease of placement
 - Placement success
 - Safety
 - Tolerability
- Discontinuation rate and reasons
- Estimated Study Completion Date: 7/20

Amphora[®]

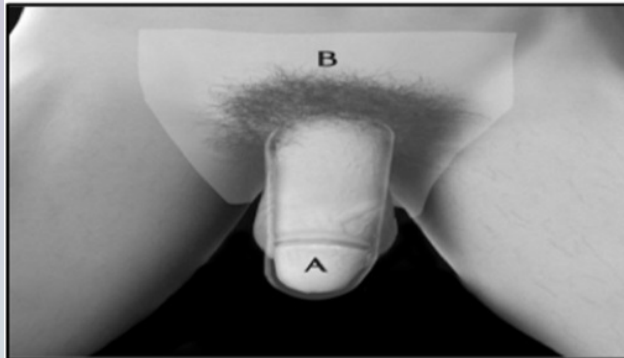
- Spermicidal contraceptive
- Does not contain nonoxynol 9
- Phase 3 study underway
- Data expected Q1 2019
- Already licensed as a lubricant
- Potential additional indications:
prevention of chlamydia, gonorrhea and
recurrent bacterial vaginosis



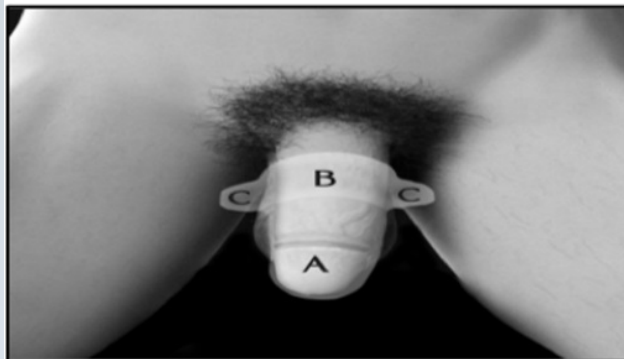
Pilot study on functional performance and acceptability of two new synthetic adhesive male condoms (Wondaleaf): a randomized cross-over trial



a) The layout of Wondaleaf-On-Man and its smaller version, Wondaleaf-Cap. The thickness of both condoms is 0.02mm.



b) Wondaleaf-On-Man duly deployed on the penis. The condom portion (A) loosely covers the penis, while the integral adhesive shield (B) sticks onto the entire groin region (including testicles).



c) Wondaleaf-Cap duly deployed on the penis. The loose-fitting condom (A) covers the glans penis, while the adhesive shield sticks onto the penile shaft (B) and onto itself (C) to form the proximal part of the condom (B) and two lateral tabs (C) respectively. The tabs that protrude laterally are soft and thin.



d) Durex-Together expanded and laid flat. It has nominal width 52.5mm, length 190mm, and thickness 0.07mm. It is pre-lubricated, and features an easy-on shape.