



# Contraceptive Update

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# Topics

- Long-acting contraception: update
- Adolescent contraception
- Postpartum IUD and Implant
- Sayana Press
- Vaginal Ring

# WHO Medical Eligibility Criteria

Can my client use  
this method?

1	Can use the method	No restrictions
2	Can use the method	Advantages generally outweigh theoretical or proven risks.
3	Should not use method unless no other method is appropriate	Theoretical or proven risks generally outweigh advantages
4	Should not use method	Unacceptable health risk

# Comparing effectiveness of contraceptive methods

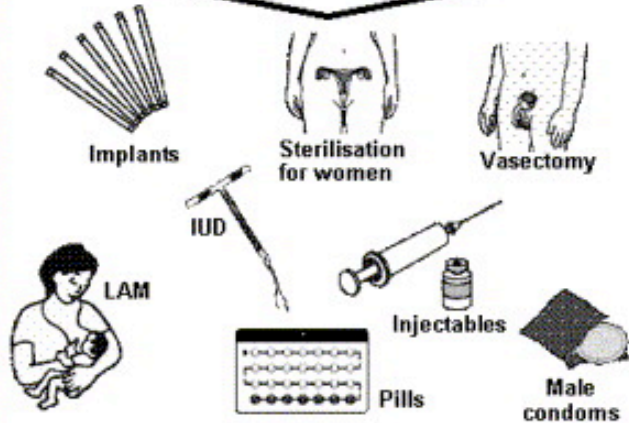
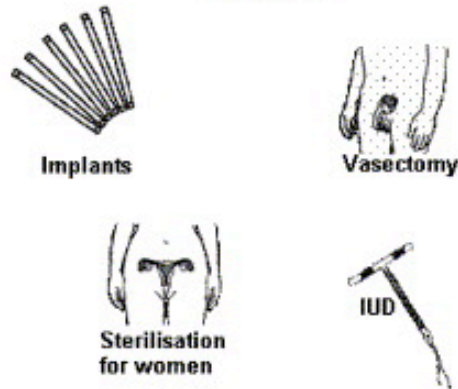
## Average users

Includes users who sometimes forget or make mistakes and users who always use the method correctly and consistently. Most people can expect this level of effectiveness.

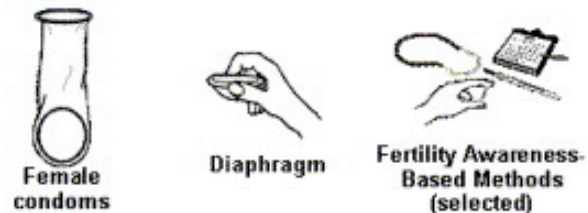
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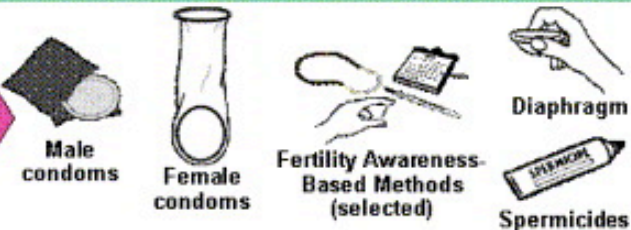
**More effective**  
2 or fewer pregnancies per 100 women in one year



**Effective**  
3 to 9 pregnancies per 100 women in one year



**Less Effective**  
10 to 30 pregnancies per 100 women in one year



Overview of  
Long-Acting  
Methods

SayanaPress

Efficacy and Continuation

## What Shall we Talk About?

Contraceptive Vaginal Rings

Adolescent  
Contraception

Postpartum IUD



# Overview of Long-Acting Methods

# LARC Methods

Pregnancy rates in first year of use  
(per 100 women)



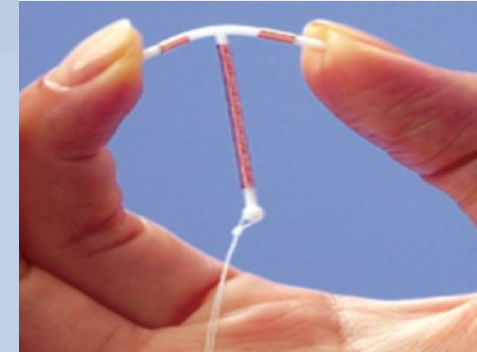
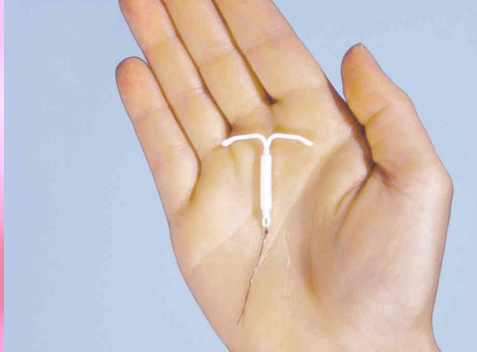
0.6



0.2



0.05

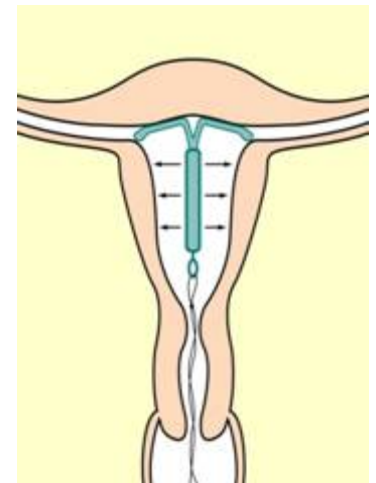


<b>(LNG-IUS)</b>	<b>(LNG-IUS)</b>	<b>(Copper T IUD)</b>	<b>(ENG-Implant)</b>
28x30mm	32x32mm	32x36mm	40x2mm
3 years	5 years	12 years	3 years
0.4% failure	0.2% failure	0.6% failure	0.05% failure
Initially releases 14mcg/day levonorgestrel → 5mcg/day (3 yrs)	Initially releases 20mcg/day levonorgestrel → 10mcg/day (5 yrs)	No hormone Copper ions	Releases 60mcg/day etonorgestrel
<ul style="list-style-type: none"> <li>-Thickens cervical mucus</li> <li>-Thins endometrial lining</li> <li>-Spermicidal</li> <li>-Incomplete ovulation suppression</li> </ul>		<ul style="list-style-type: none"> <li>-Spermicidal</li> <li>-Change in ovum transport speed</li> </ul>	<ul style="list-style-type: none"> <li>-Suppresses ovulation</li> <li>-Thickens cervical mucous</li> </ul>

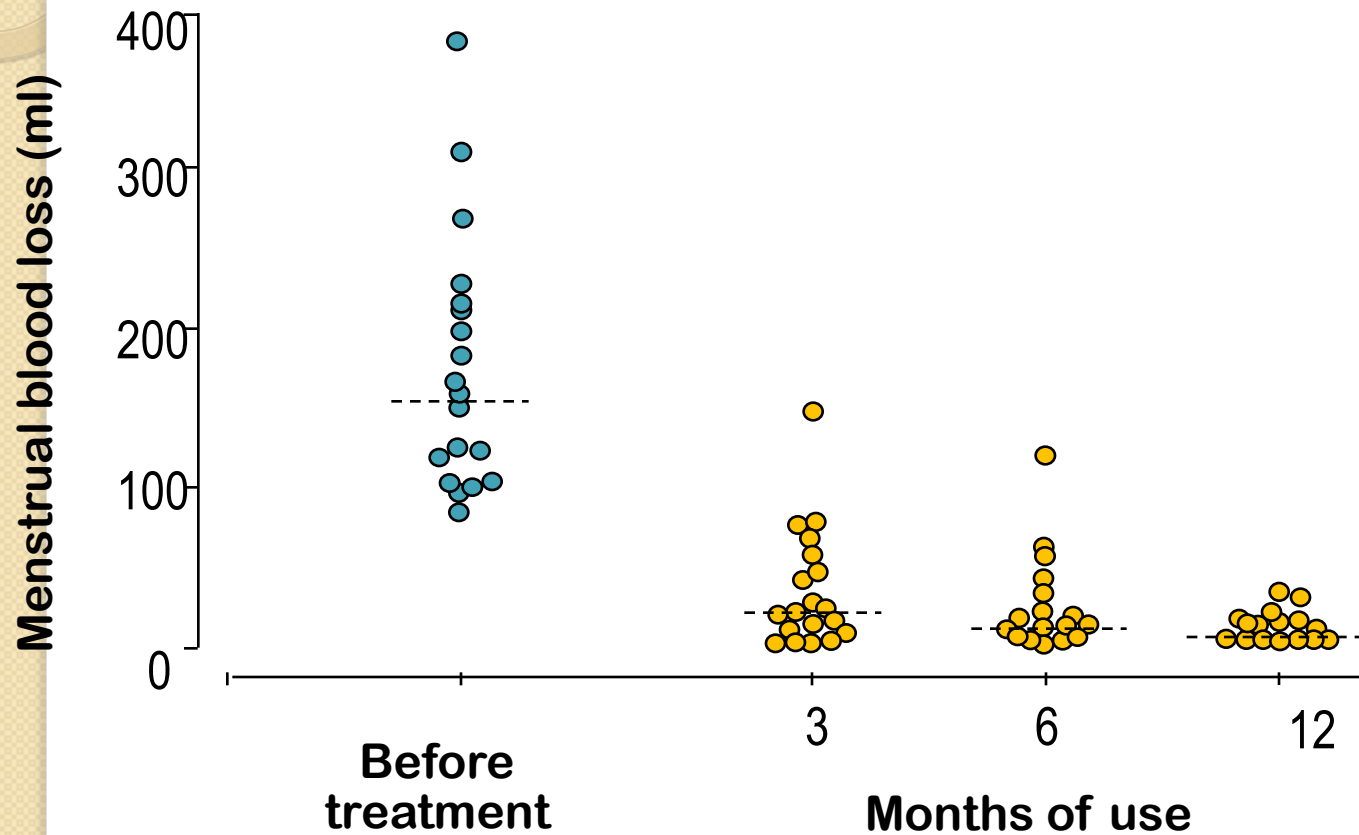


# IUDs: Mechanism

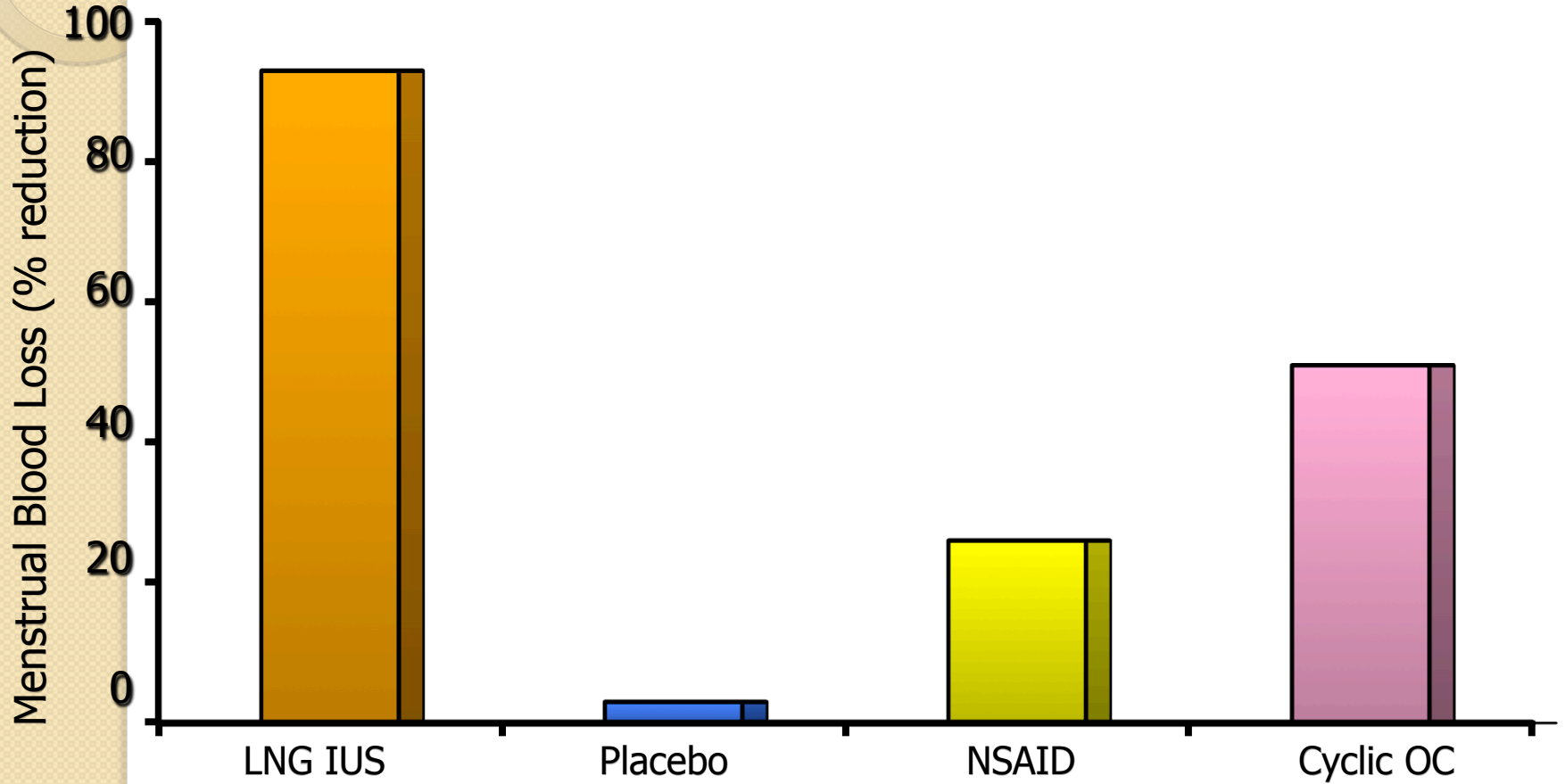
- Mechanism: primarily by preventing fertilization
  - Copper has direct effects on uterus, sperm and ova
  - Levonorgestrel:
    - THICKENS cervical mucus
    - THINS endometrial lining



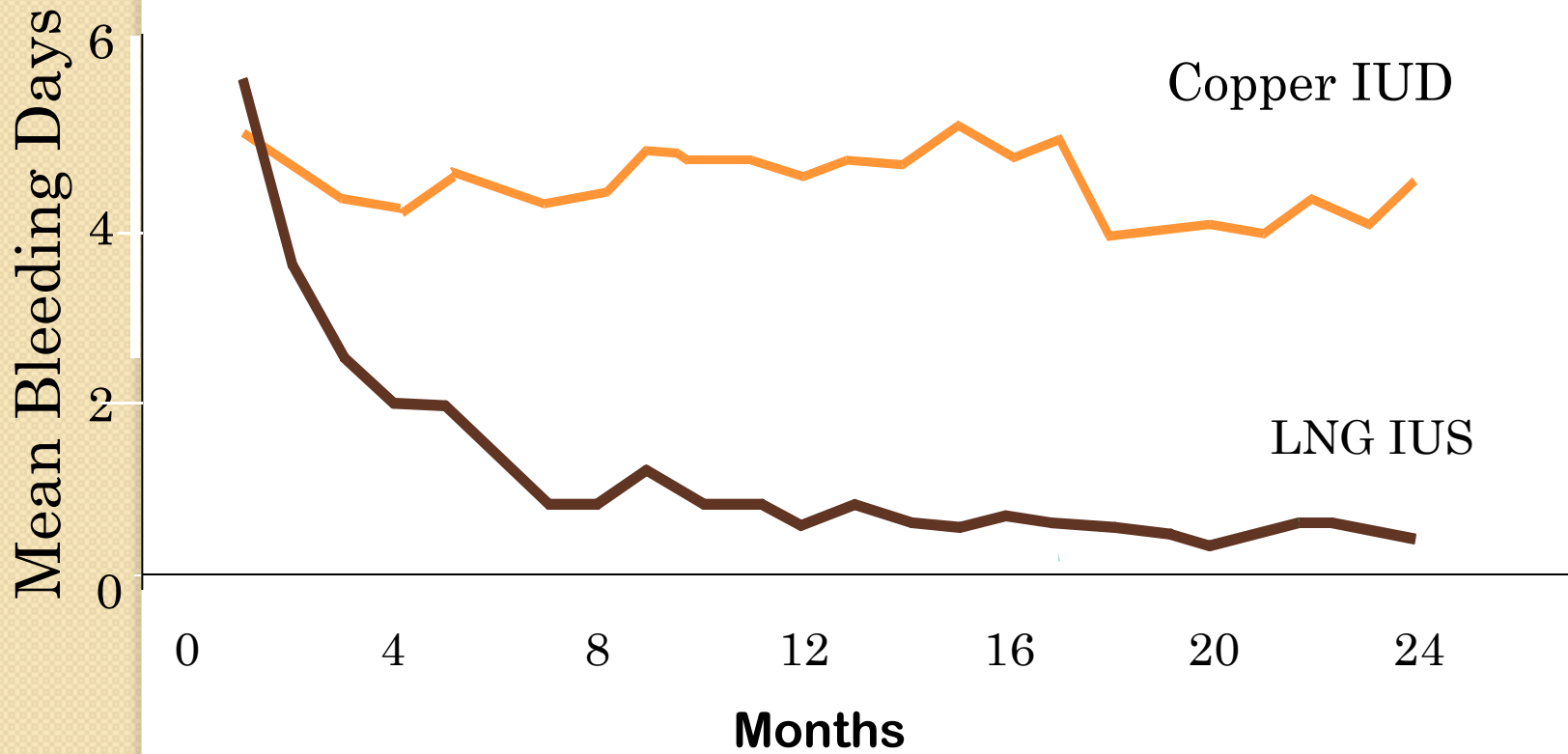
# LNG IUD: Treatment Heavy Bleeding



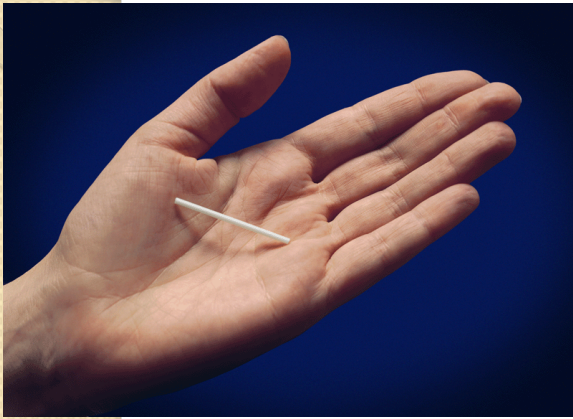
# LNG IUD: reduction in menstrual blood loss



# IUDs



# Implanon/Nexplanon™ Etonogestrel Implants



- Progestin-only method
- 4 x 0.2cm
- Prevents ovulation
- Long-acting (3 years)
- Main side-effect is unpredictable menstrual cycles
- Fertility returns within a few days of removal
- Highly effective

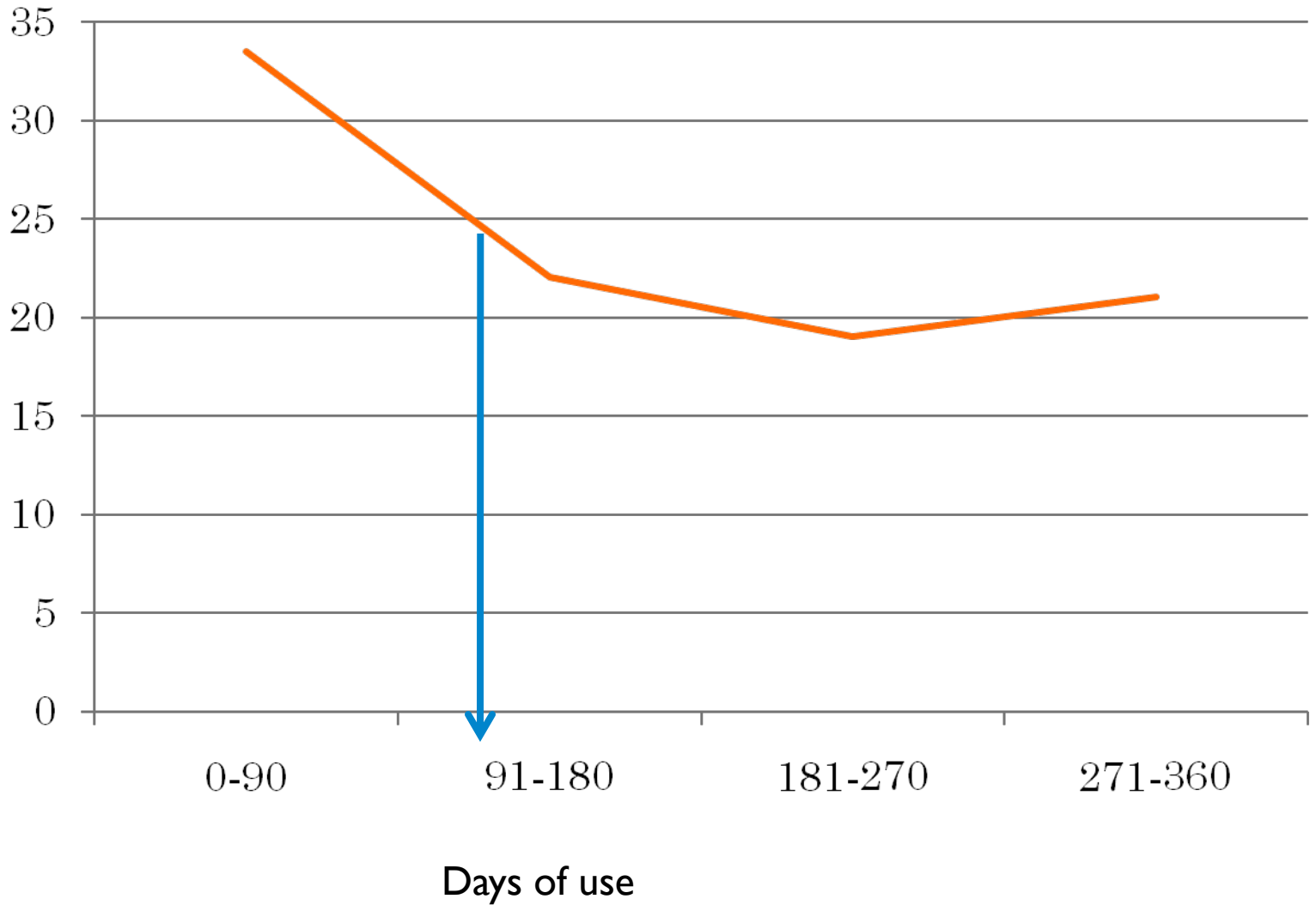


## Zarin® (Sino-implant II)

- Subdermal Contraceptive Implant
- Levonorgestrel

# IMPLANT

Median number of bleeding/spotting days



# Comparison of Hormonal Implants

	Jadelle	ImplanonNXT	Sino-implant (II)/Zarin
<b>Manufacturer</b>	Bayer Healthcare	Merck/MSD	Shanghai Dahua Pharmaceutical Ltd.
<b>Formulation</b>	150 mg levonorgestrel in 2 rods	68 mg etonogestrel in 1 rod	150 mg levonorgestrel in 2 rods
<b>Mean Insertion &amp; Removal time</b>	Insertion: 2 min Removal: 5 min	Insertion: 1 min Removal: 2-3 min	Insertion: 2 min Removal: 5 min
<b>Labeled duration</b>	5 years	3 years	4 years
<b>Trocars</b>	Autoclavable and Disposable	Pre-loaded disposable	Disposable
<b>Cost of implant (US\$)<sup>1</sup></b>	\$8.50 (↓\$19.00)	\$16.40 (↓\$18.00)	\$8.50
<b>Cost per Year (if used for duration)</b>	\$1.70	\$5.50	\$2.13
<b>WHO Prequal</b>	Yes	Yes	Application submitted

<sup>1</sup> FOB price in country of origin.





# **Efficacy and Continuation**

# Comparing effectiveness of contraceptive methods

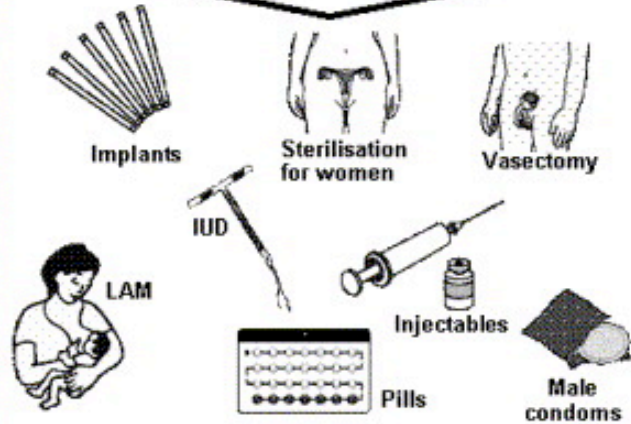
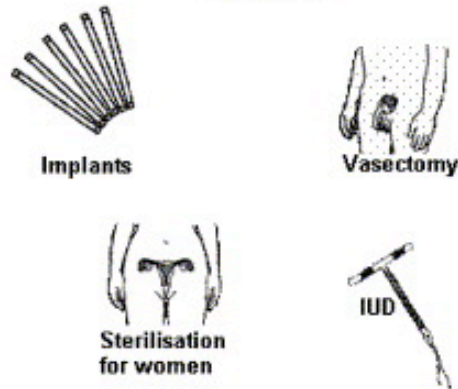
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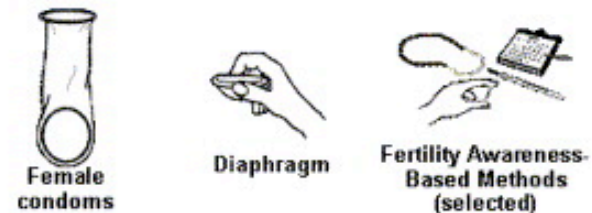
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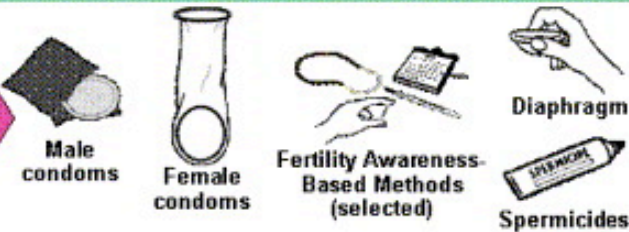
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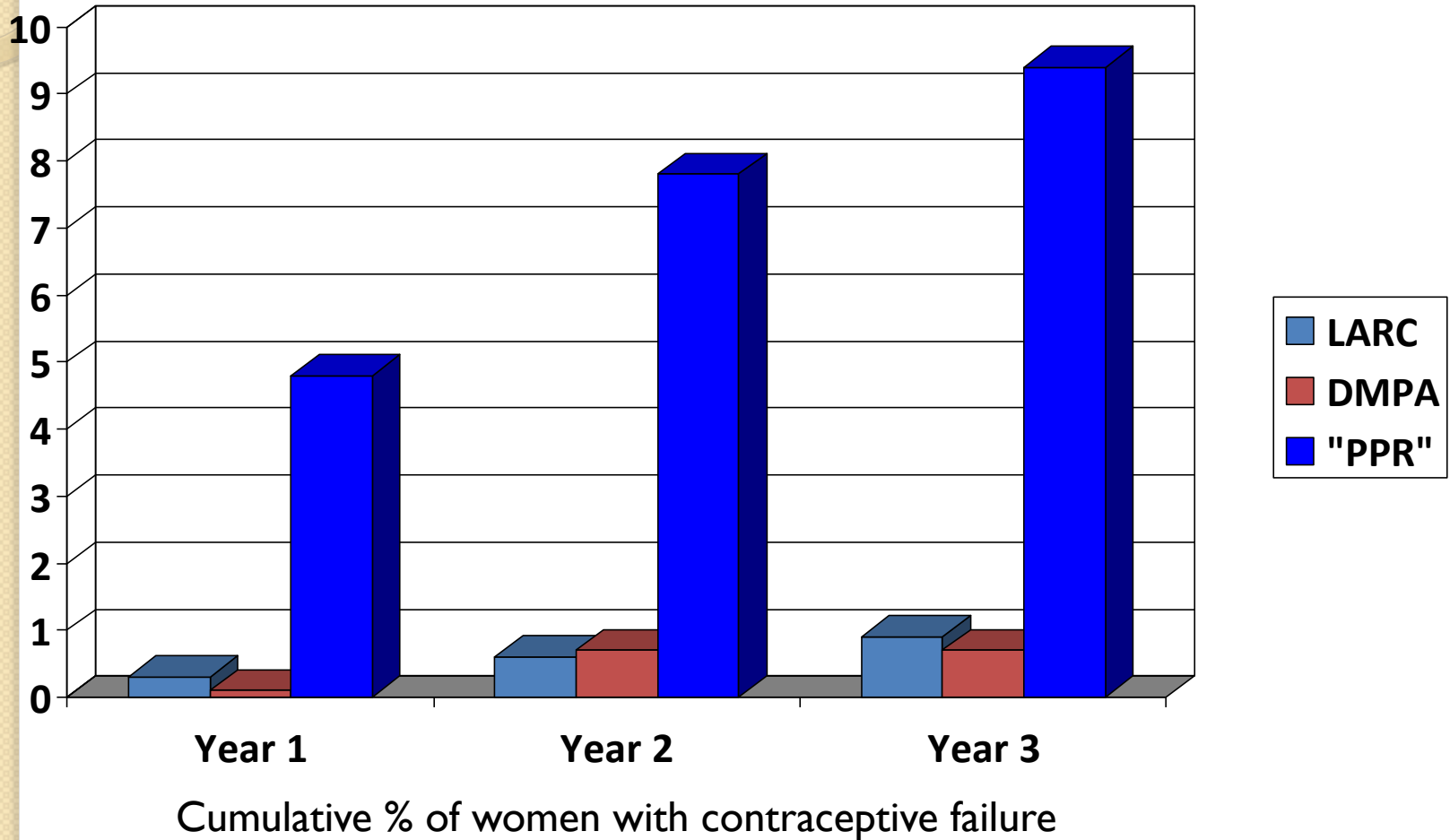
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3 to 9 pregnancies per 100 women in one year



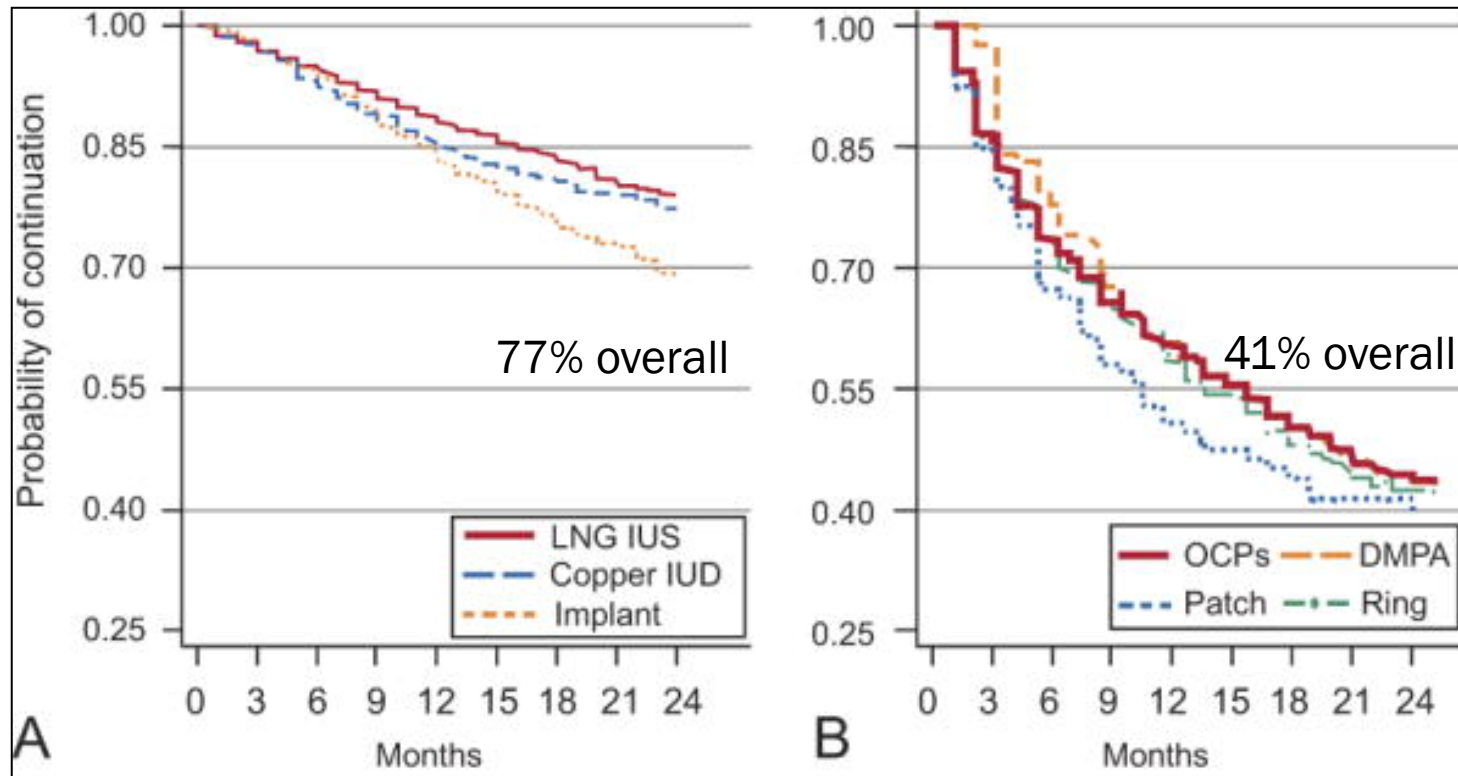
**Less Effective**  
10 to 30 pregnancies per 100 women in one year



# Contraceptive Failure: LARC vs. the rest

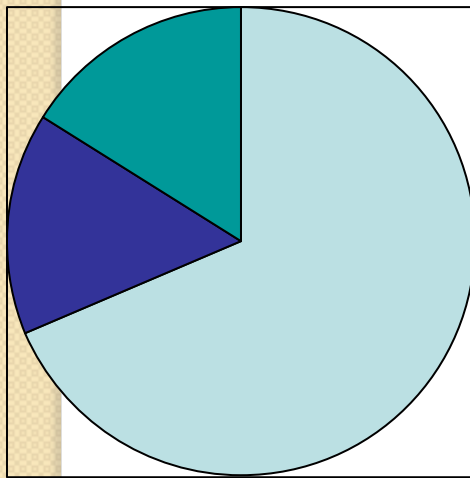


# Continuation over 24 months

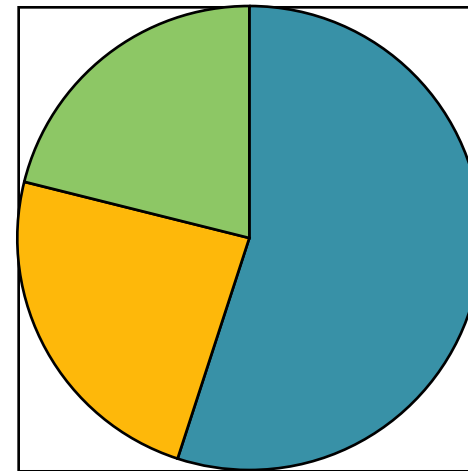


**Twenty-Four-Month Continuation of Reversible Contraception.** O'Neil-Callahan, Micaela; Peipert, Jeffrey; MD, PhD; Zhao, Qihong; Madden, Tessa; MD, MPH; Secura, Gina; PhD, MPH  
Obstetrics & Gynecology. 122(5):1083-1091, November 2013. DOI: 10.1097/AOG.0b013e3182a91f45

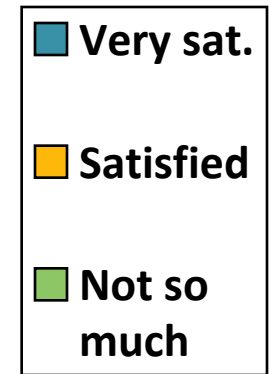
# Satisfaction is high



IUD (N= 2,324)



Implant (N=522)



# 2-visit protocols?

- Rationale: pre-screen for STD?
  - Risk of PID in large IUD cohort was 0.0054
  - Similar whether screened for Chlamydia/ Gonorrhea or not
  - For women <26 years old, same-day screening same as pre-screening
  - For >26 years old, NO screening = ANY screening

If all answers  
are

## PREGNANCY CHECKLIST

If any answer is

**NO**

...then cannot  
rule out  
pregnancy

Did you have a baby less than 6 months ago, are you fully or nearly-fully breastfeeding, and have you had no menstrual period since then?

Have you abstained from sexual intercourse since your last menstrual period or delivery?

Have you had a baby in the last 4 weeks?

Did your last menstrual period start within the past 7 days (or within the past 12 days if you are planning to use an IUD)?

Have you had a miscarriage or abortion in the past 7 days (or within the past 12 days if you are planning to use an IUD)?

Have you been using a reliable contraceptive method consistently and correctly?

**YES**

...then can be  
reasonably sure  
she is not  
pregnant



# Adolescents and Contraception



# Adolescents: Rights-focused approach

Recommend eliminating **financial barriers** to contraceptive use

Recommend interventions to **improve access** to comprehensive contraceptive information and services for users and potential users with difficulties in accessing services (e.g., adolescents).

Recommend provision of sexual and reproductive health services, including contraceptive information and services, for adolescents without **mandatory parental and guardian authorization/notification**.



WHO, Ensuring Human Rights in the provision of contraceptive information and services  
Guidance and recommendations, 2014

# WHO Guidance

- In general, adolescents are eligible to use any method of contraception and must have access to a variety of contraceptive choices.
- Age alone does not constitute a medical reason for denying any method to adolescents.
- While some concerns have been expressed regarding the use of certain contraceptive methods in adolescents these concerns must be balanced against the advantages of avoiding pregnancy.

# WHO Guidance

- Consider:
  - Social and behavioral context (example: STI risk)
  - Daily regimens more challenging than for adults
  - Sporadic patterns of sexual intercourse
  - Need to conceal (married vs. unmarried)
- Counseling is very important

# WHO MEC Recommendations

Contraceptive Method	MEC Category
Combined hormonal methods	1
Injectable	2 (1)
Progestin-only pill	1
Implant	1
IUD	2
Barrier	2
Emergency Contraceptive Pills	OK

# Safety Concerns – Bone Density

- DMPA has been associated with decreased bone mineral density (BMD) in adolescent users, but BMD returns to baseline within 12 months of stopping DMPA
  - What about fracture risk?
- WHO
  - There should be no restriction on the use of DMPA, including no restriction on duration of use, among women aged 18-45 years who are otherwise eligible to use the method
  - Among adolescents (menarche – age 18), advantages generally outweigh theoretical safety concerns
  - Recommendations regarding DMPA use also pertain to the use of NET-EN

# Other Considerations

- Weight gain in adolescents using DMPA?
  - Obese adolescents may be more likely to gain weight
  - Obese adolescents:
    - DMPA is Category 2, NET-EN is Category I
- Use of combined methods in obese adolescents?
  - Inconsistent reports of weight gain
  - Inconsistent evidence of decreased efficacy in obese women
  - They'll gain more weight in pregnancy...

# Adolescents and IUDs

- Similar continuation rates
  - 87% vs. 89% in large study (12 months)
  - 2-3% discontinued due to adverse event
- Similar (LOW) complication rates
  - Pregnancy risk?
- IUD type may matter
  - LNG IUD has favorable effects on menstrual bleeding

# Other Considerations: IUD

Condition	MEC Category
Nulliparity	2
Current PID	4 (I - don't insert) 2 (C - don't need to remove)
Current purulent cervicitis, chlamydial infection, gonorrhoea	4 (I) 2 (C)
Other STIs / Vaginitis	2
Increased risk of STI	2/3
High risk of HIV	2



# CHOICE project

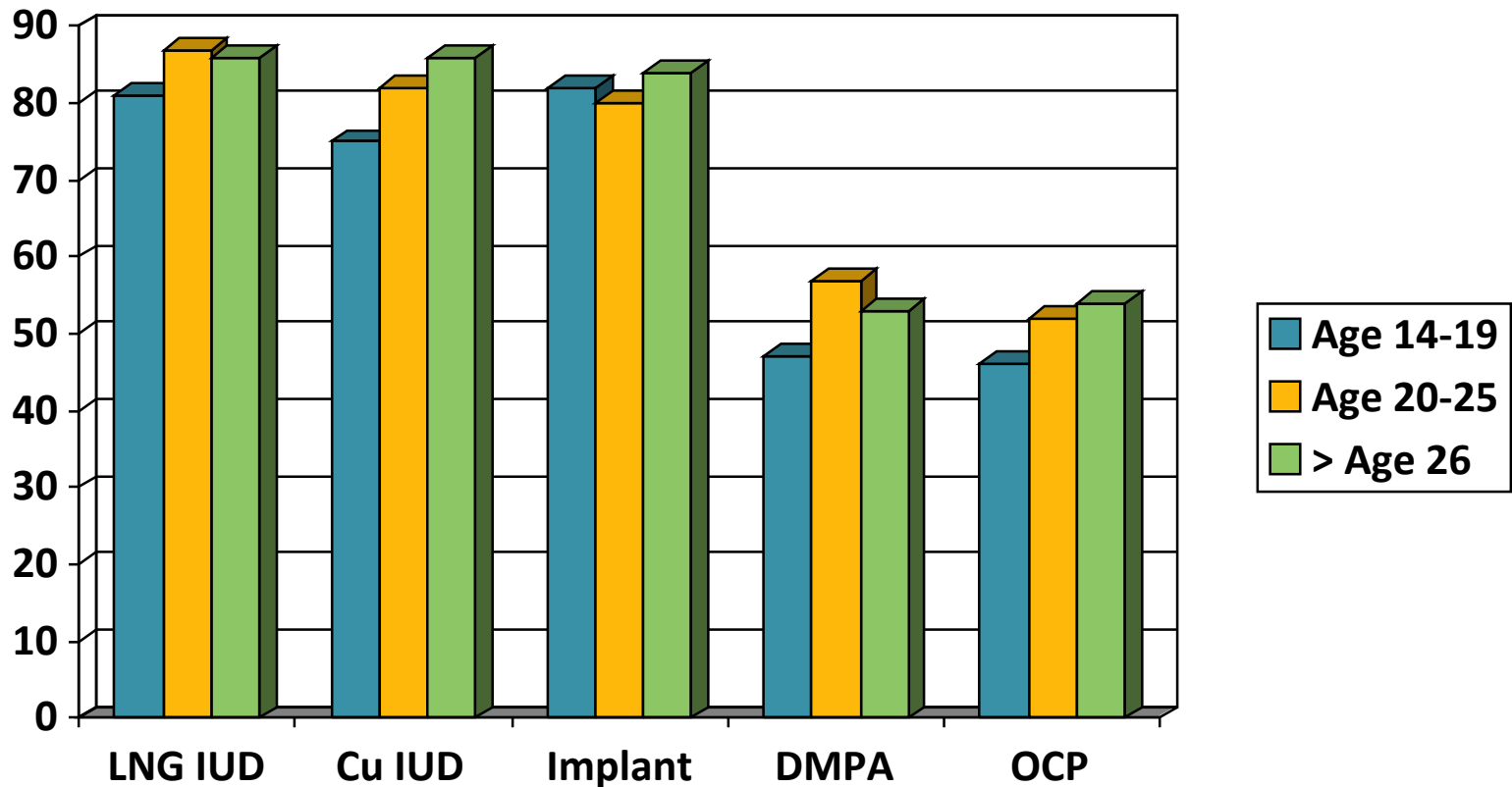
- **Who:** 10,000 women age 14-45 who want to avoid pregnancy for at least 1 year
- **What:** Provision of no-cost contraception for 3 years
- **When:** 2007-2011
- **Why:** to increase LARC awareness and utilization
  - LARC = Long-acting Reversible Contraception
  - (IUDs and implants)

# CHOICE Findings: Adolescents

- 62% (658/1054) chose LARC method
- Factors that influenced choice of LARC:
  - Prior unintended pregnancy
  - Financial resources
  - Not race or education level

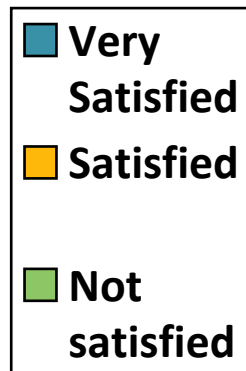
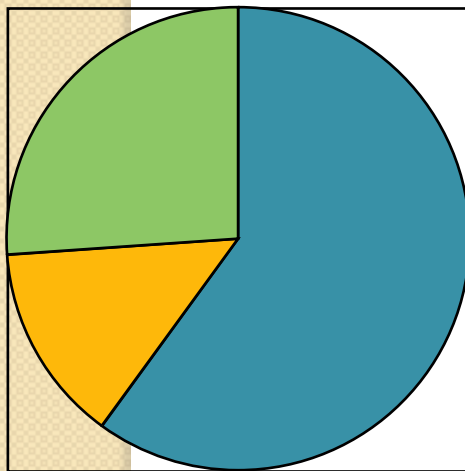


# 1-year Contraceptive Continuation Rates

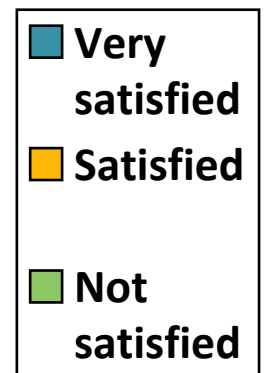
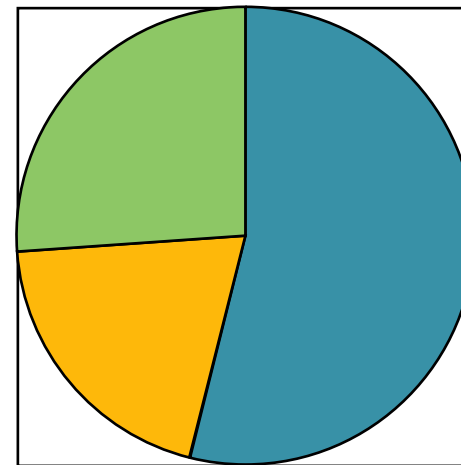


Rosenstock, et al, OBG 2012

# Adolescents' satisfaction with LARC Methods

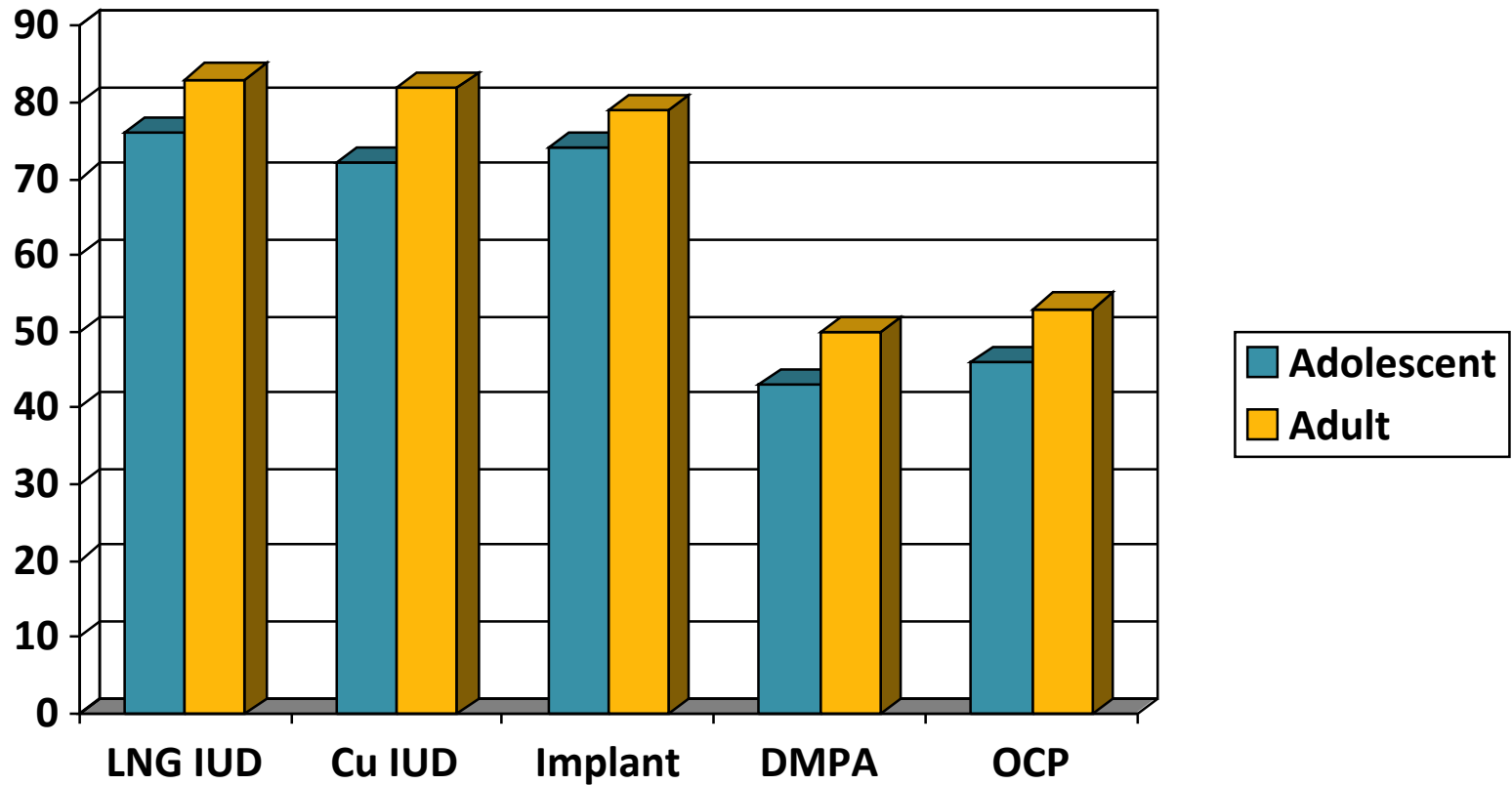


IUD (N= 2,324)



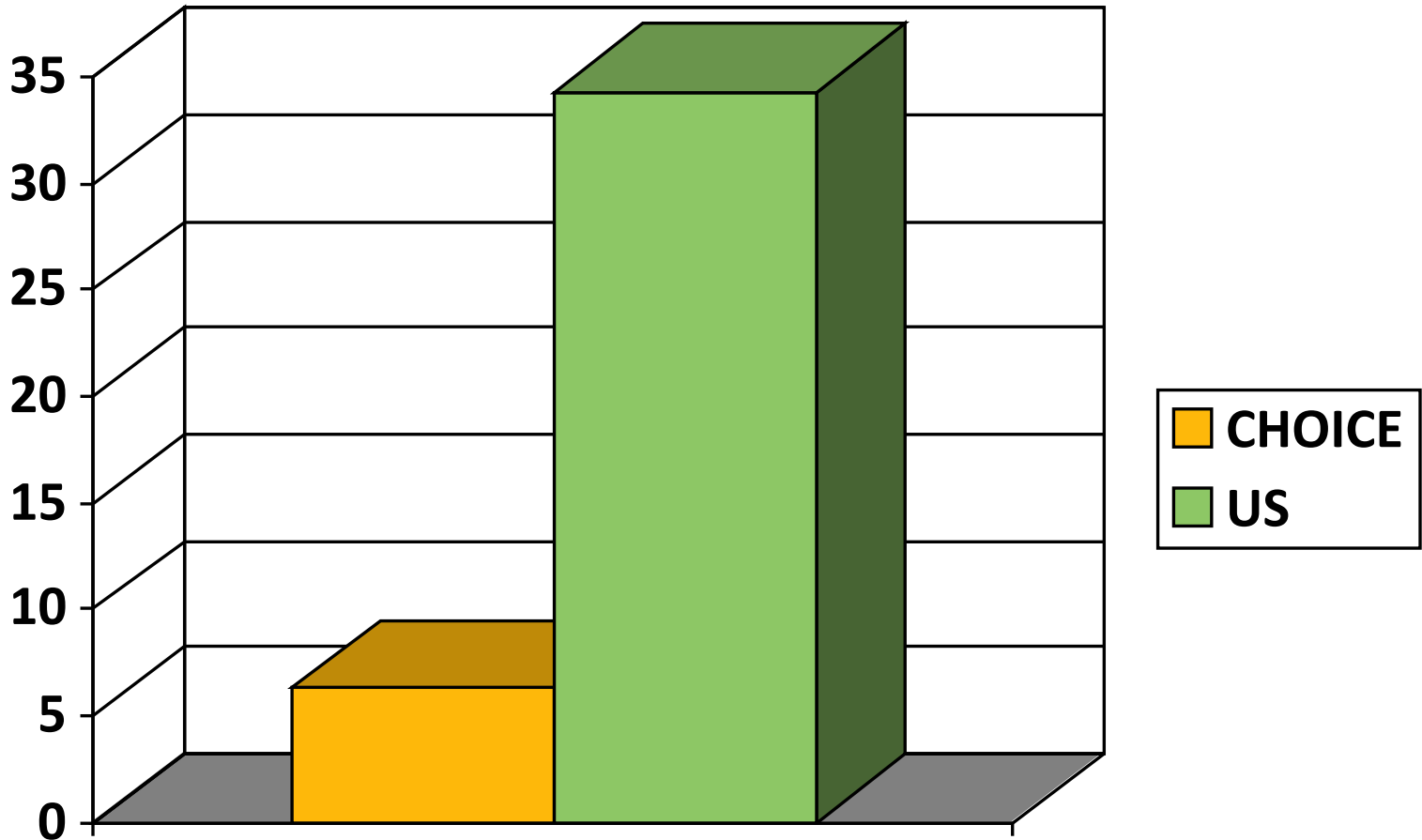
Implant (N=522)

# Adolescents' Satisfaction with Contraceptive Methods



Rosenstock, et al, 2012

# Teen Birth Rates in US



**Teen births, 2010**

Births per 1,000 teens, ages 15-19



# Postpartum IUD

# Postpartum Contraception: Individual Considerations



Benefits  
Immediate initiation

Risks  
Immediate initiation

**Patient  
preference**

35% of women do not return for follow-up visit.



# Importance of Birth Spacing

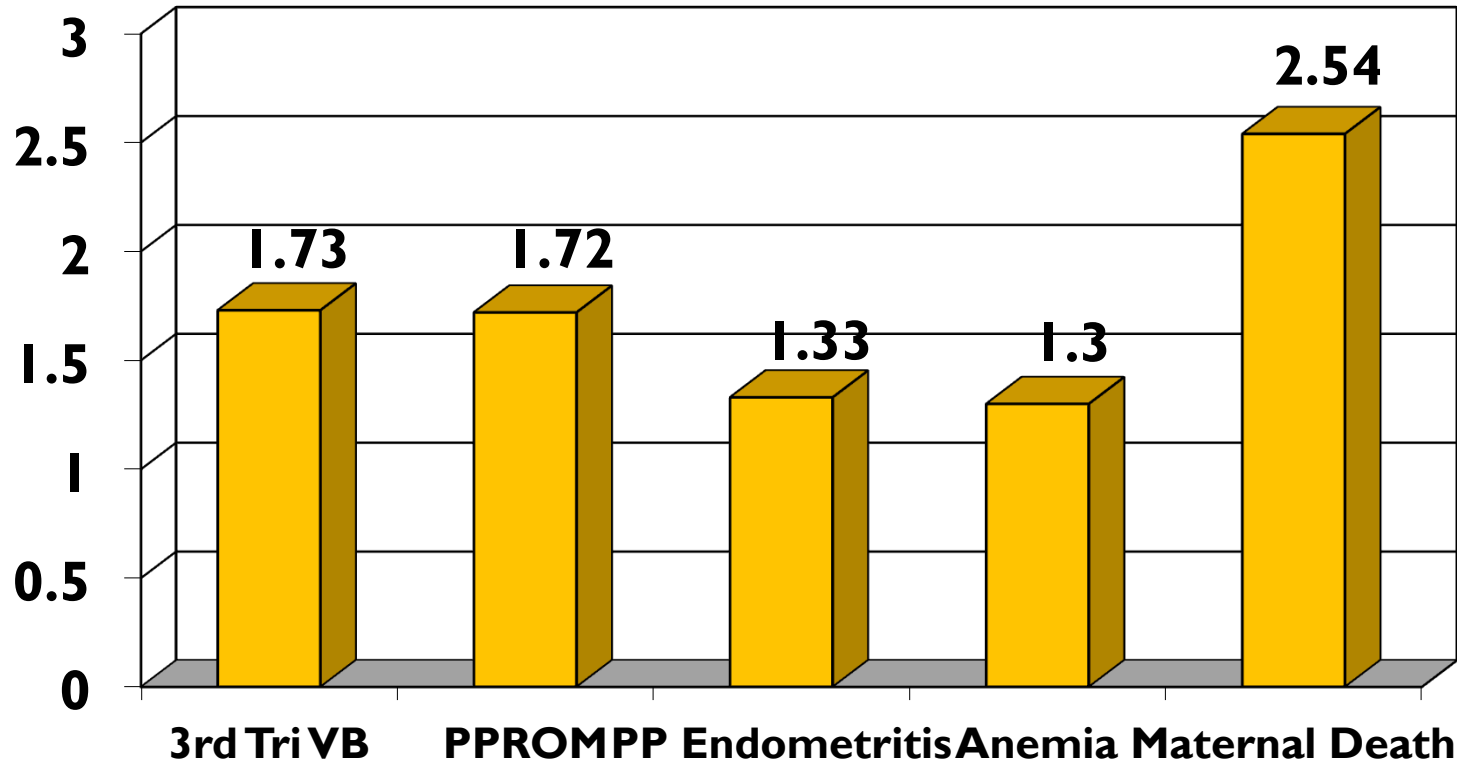
- **Developing countries:**
  - 40% do not obtain contraception within 1 yr.
- **United States:**
  - 12% are using no method and 7% low-efficacy method in 9 mos.



Ross & Winfrey 2001 IFPP  
Conde-Agudelo et al 2000 BMJ  
<http://www.cdc.gov>  
MMWR Morb Mortal Wkly Rep, 2009  
Fanello et al 2007 J Gynecol Obstet

# Effect of Short Inter-pregnancy Intervals

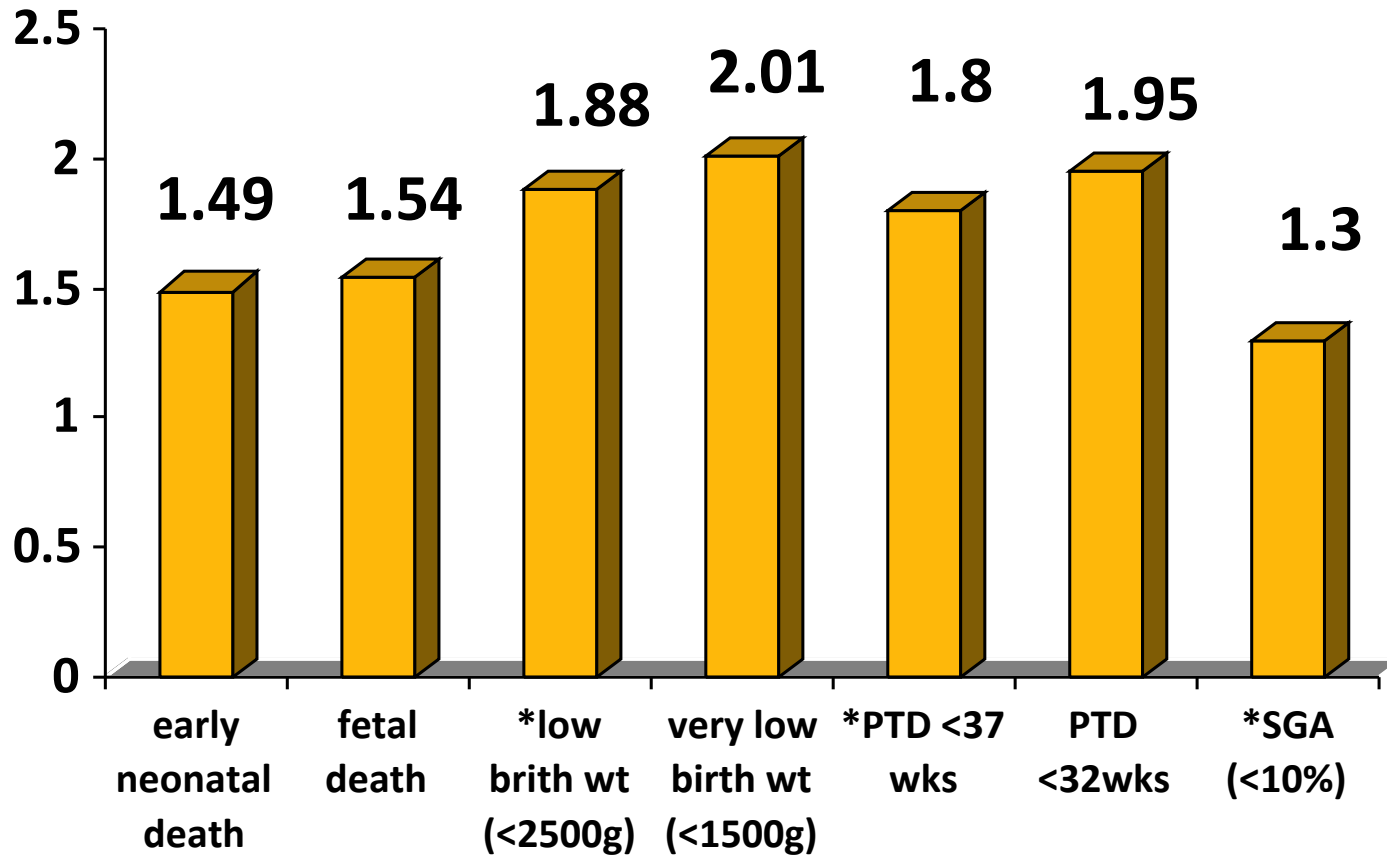
## Obstetric Outcomes



Odds Ratio at pregnancy intervals of <6 months vs. 18-23 months

N=500,000

# Effect of Short Inter-pregnancy Intervals Neonatal Outcomes



Odds Ratio at pregnancy intervals of <6 months vs. 18-23 months  
N=1.2 million

# Definitions

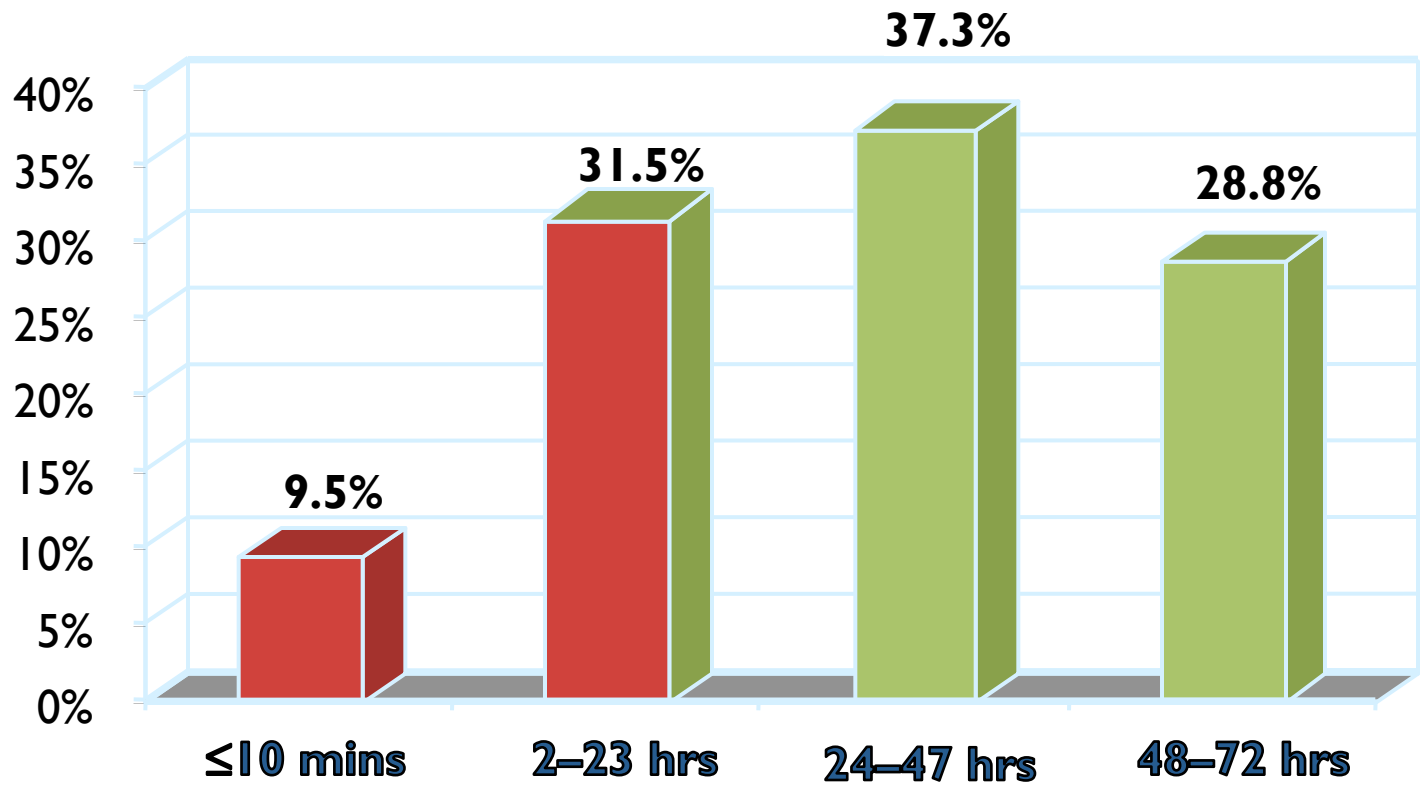
- Immediate post-placental/postpartum (IPP) IUD insertion: IUD insertion within 10 minutes of delivery of the placenta
- Early postpartum (EP) period: 10 minutes to 48 hours after delivery
- Interval (INT) IUD insertion: 4-8 weeks postpartum



# Why 10 minutes?

## Postpartum IUD Insertion

Adjusted Cumulative  
Expulsion Rates



p<0.001 (≤10 minutes compared to all other groups)

# WHO Medical Eligibility for Contraceptive Use

Postpartum*	LNG IUS	Copper IUD
<10 minutes after delivery of the placenta	1/3	1
10 minutes after delivery of the placenta to <4 weeks	3	3
≥4 weeks	1	1
Puerperal sepsis	4	4

\*including post-Cesarean section

# CDC Medical Eligibility for Contraceptive Use

Postpartum*	LNG IUS	Copper IUD
<10 minutes after delivery of the placenta	2	1
10 minutes after delivery of the placenta to <4 weeks	2	2
≥4 weeks	1	1
Puerperal sepsis	4	4

\*Breastfeeding or non-breastfeeding women, including post-Cesarean section

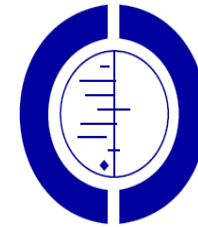
Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use, 2010. MMWR May 2010;59:1-86.

# Cochrane Review 2010

- Nine trials
- No increase in infection, bleeding, or perforation
- Expulsion rates are higher for immediate versus delayed insertion

Immediate post-partum insertion of intrauterine devices  
(Review)

Grimes D, Schulz K, van Vliet H, Stanwood N



THE COCHRANE  
COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2005, Issue 3

<http://www.thecochranelibrary.com>



Immediate post-partum insertion of intrauterine devices (Review)  
Copyright ©2005 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd



# Does it stay in? (Turkey)

Immediate postplacental insertion of CuT 380 model (n = 235)

	6 Weeks (n = 221)	6 Months (n = 210)	12 Months (n = 183)
Removals for			
Bleeding/pain	0.3	2.8	3.1
Other medical reasons	0.1	0.8	1.1
Planned pregnancy	0.1	1.1	4.8
Personal reasons	0.5	0.8	2.1
Unplanned pregnancy	0.0	0.2	0.3
Expulsion rate	5.1	7.0	12.3
Continuation rate	94.3	87.6	76.3

Values are gross cumulative event rates per 100 users up to 12 months.

Did not separate out c/s vs. vaginal delivery

# Does it stay in? (Zambia)

- Cohort study of 1310 Copper T IUDs placed in Zambia Feb 2009-April 2010 placed after delivery but before discharge
- IUDs placed by 10 midwives
- Follow up at 6 months and 12 (51.6% follow up)



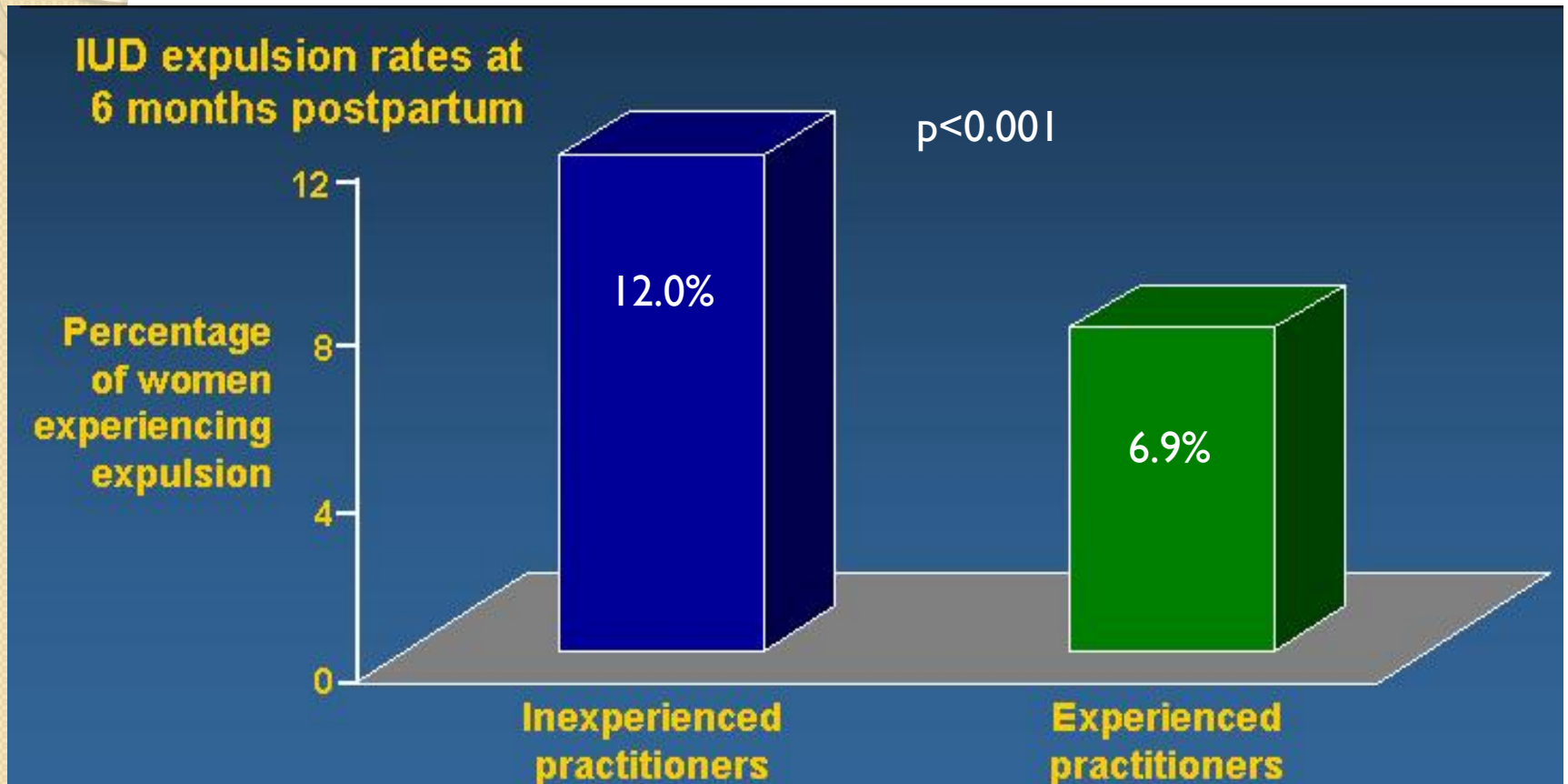
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- Results

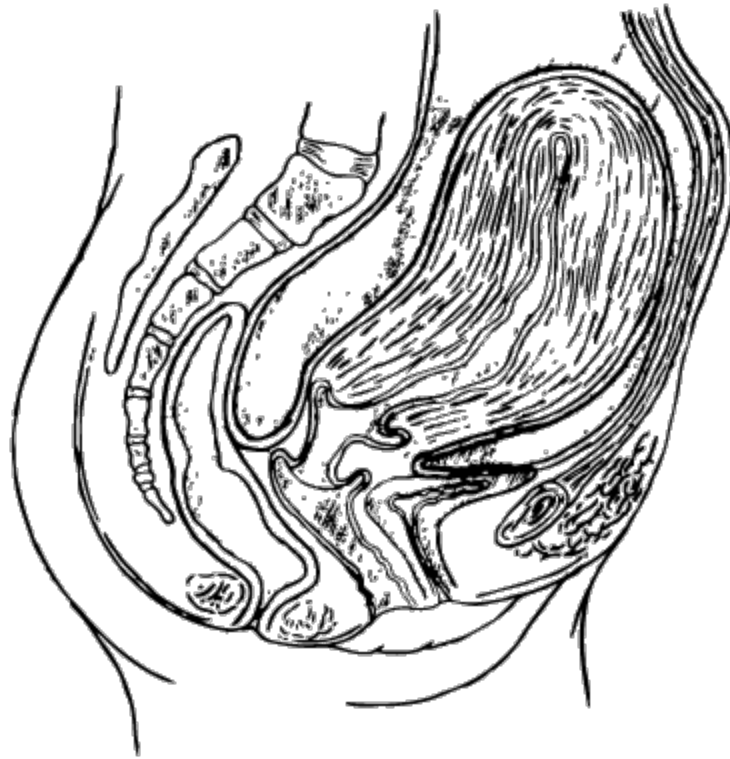
- Timing: when was it inserted?
  - 24.6% post-placental
  - 71.1% Post Partum (or “*MADIUD*” Morning After Delivery)
- Expulsion and continuation
  - **5.6% expulsion (10.8% Post Placental, 4.1% MADIUD)**
  - 3% requested removal
- Safety: No adverse events

# Why difference in expulsion?

## Provider Experience



# Uterus, Immediately Postpartum



# Delivery related conditions that may increase infection risk

- Prolonged rupture of membranes
- Prolonged labor
- Puerperal genital infection
- Puerperal sepsis



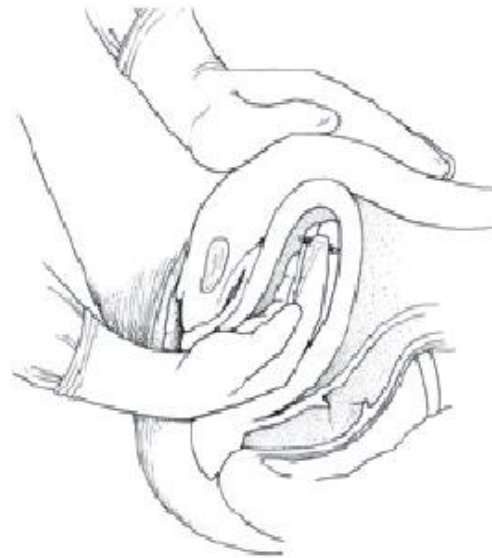
**These conditions may predispose to endometritis so consider IUD insertion at 4-6 weeks postpartum**

# PP IUC: Techniques

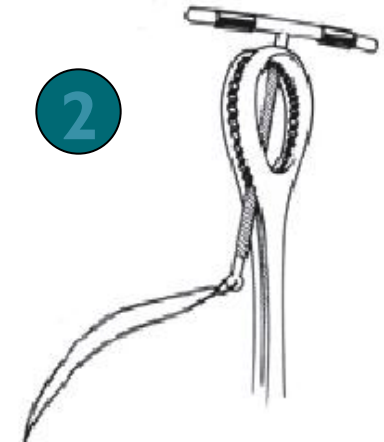
Two techniques of postplacental IUD insertion and proper location of IUD after insertion



A) IUD strings placed in palm of hand



B) Manual insertion at top of fundus



Ring only with copper IUC - for LNG use inserter



**Sayana Press**



# Sayana Press:

Depo-subQ Provera 104, for delivery with Uniject device



Depo-subQ Provera 104:

- New formulation for subQ injection
- 30% lower dose (104 mg vs. 150 mg)
- Rapid onset of action
- Same effectiveness, same length of protection (>3 months)

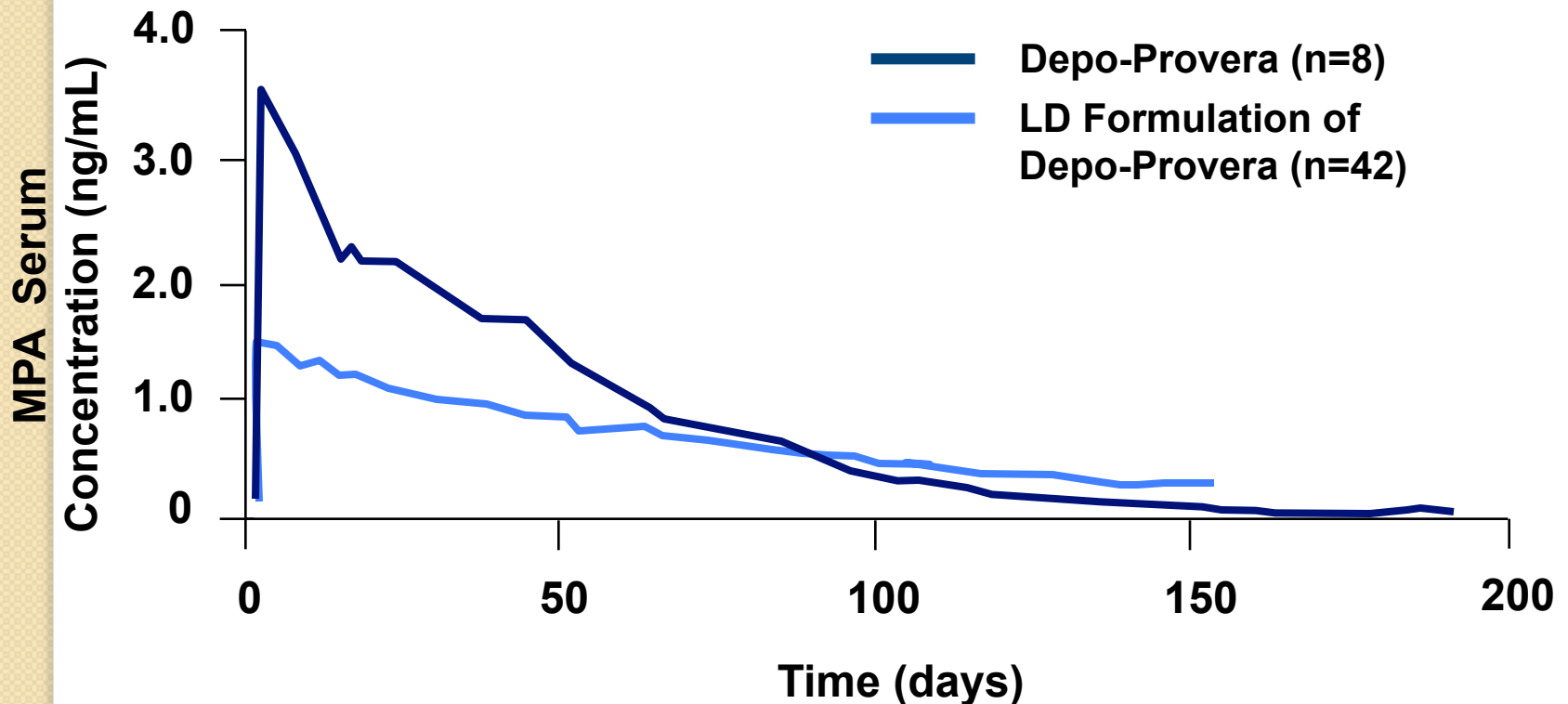
# DepoProvera<sup>®</sup>: Medroxyprogesterone acetate

- Given every 3 months
- Mechanism:
  - Suppresses ovulation
  - Thickens cervical mucus
  - Thins endometrium
- Intramuscular injection



# The LD Formulation of Depo-Provera Is Efficacious at Lower Peak Concentrations

Pharmacokinetic Profiles of the LD Formulation of Depo-Provera and Depo-Provera Contraceptive Injection



LD = lower dose.

Data on file.

## New formulation of Depo-Provera: Depo-subQ Provera 104, for delivery with Uniject



### Uniject (Sayana Press):

- ▼ Single dose, single package
- ▼ Prefilled, sterile, non-reusable
- ▼ Short needles for subQ injection (easier use by non-clinical personnel/CHWs)
- ▼ Compact; easy to use and store
- ▼ Potential for home- and self-injection
- ▼ Approval by EMA and LDC registration forthcoming

# Sayana Press: a long road



Keith B, et al., Contraception, Volume 89, Issue 5, 2014, 344 - 351

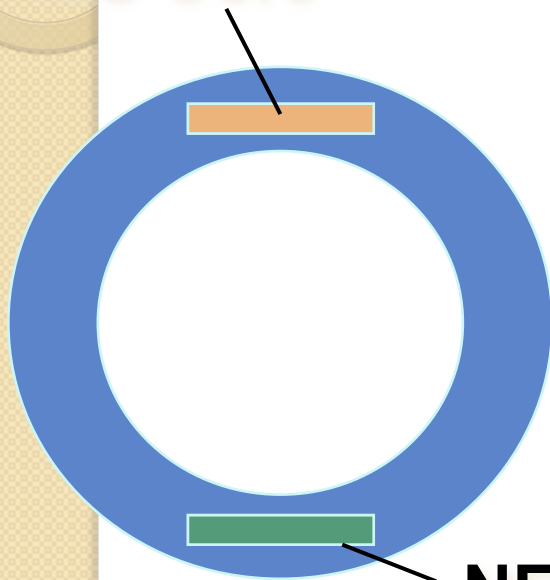
- Started in the 1990s!
- Safety and efficacy well shown
- Introduction activities in several countries
- Not intended to replace IM DMPA
  - Cost concerns



# Vaginal Rings

# Nestorone® / Ethinyl Estradiol CVR

**NES Core**



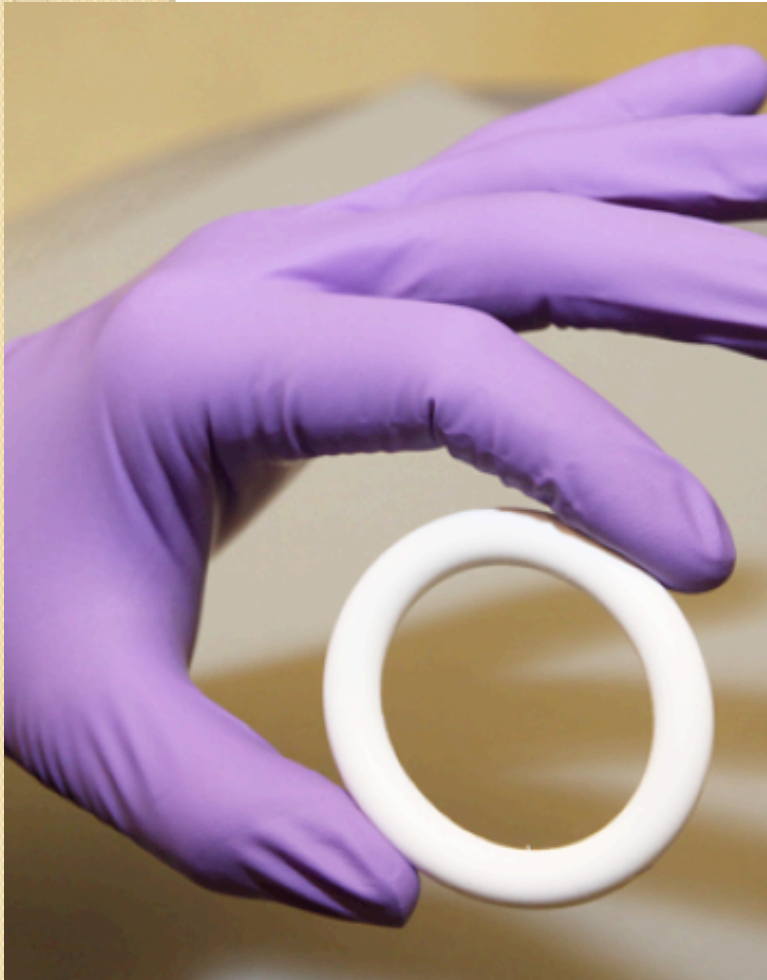
\*Delivers NES/EE 150/15µg /day,  
13 cycles 3 weeks on followed  
by 1 week off

*Developed by the Population Council  
Sponsored by USAID, NICHD, WHO*

**NES / EE Core**

**8.4 mm (3/8" ) in cross section  
58 mm (2 1/4" ) in diameter**

# Nestorone/Ethinyl Estradiol CVR (Contraceptive Vaginal Ring)



- Use for 1 year
  - In for 21 days, remove for 7
  - 13 Cycles of use
- Effective, safe
- 2 1/4 inches (~6cm) in diameter
- No refrigeration
- Woman-controlled

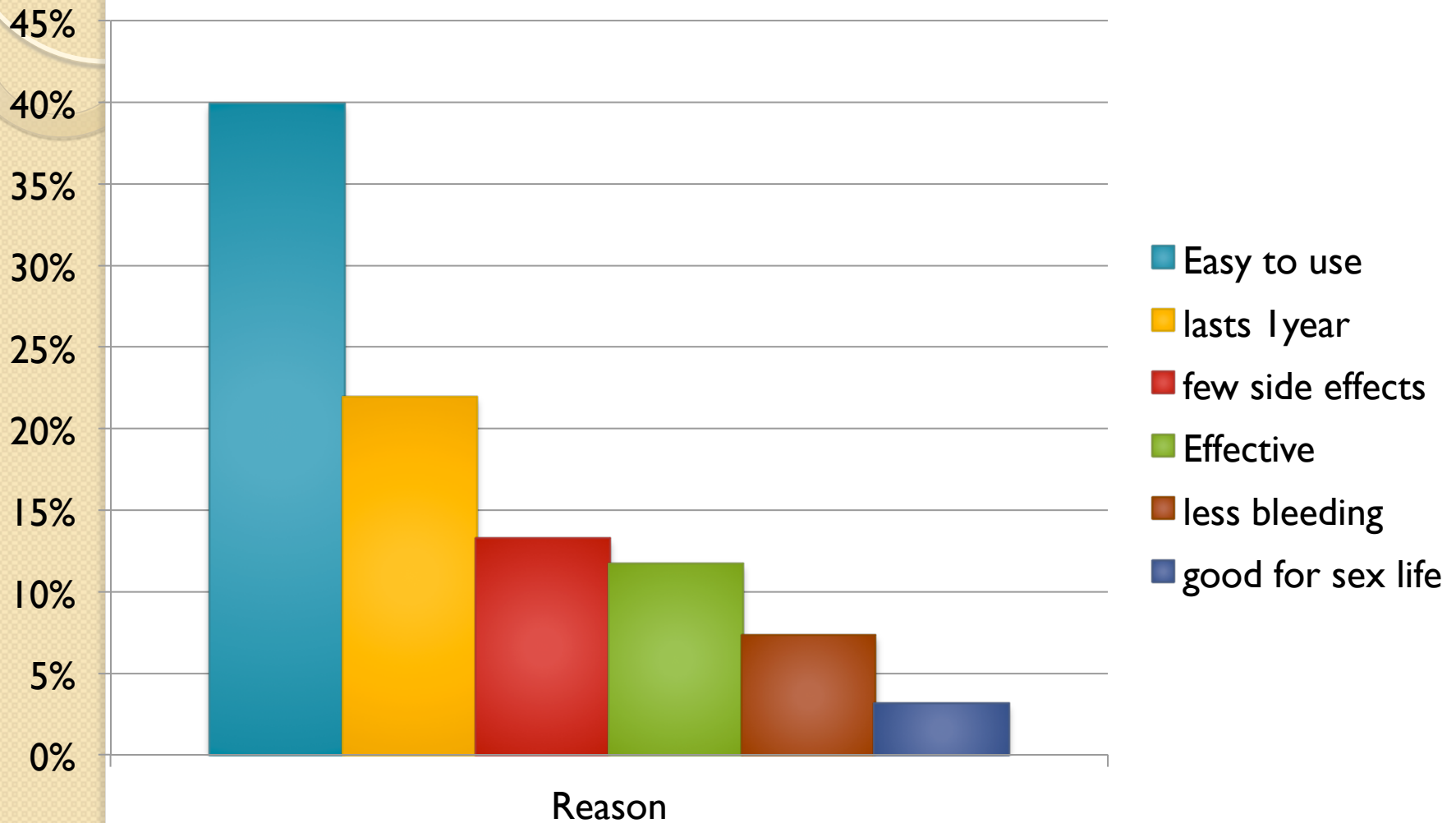


# Progesterone Ring (PVR)

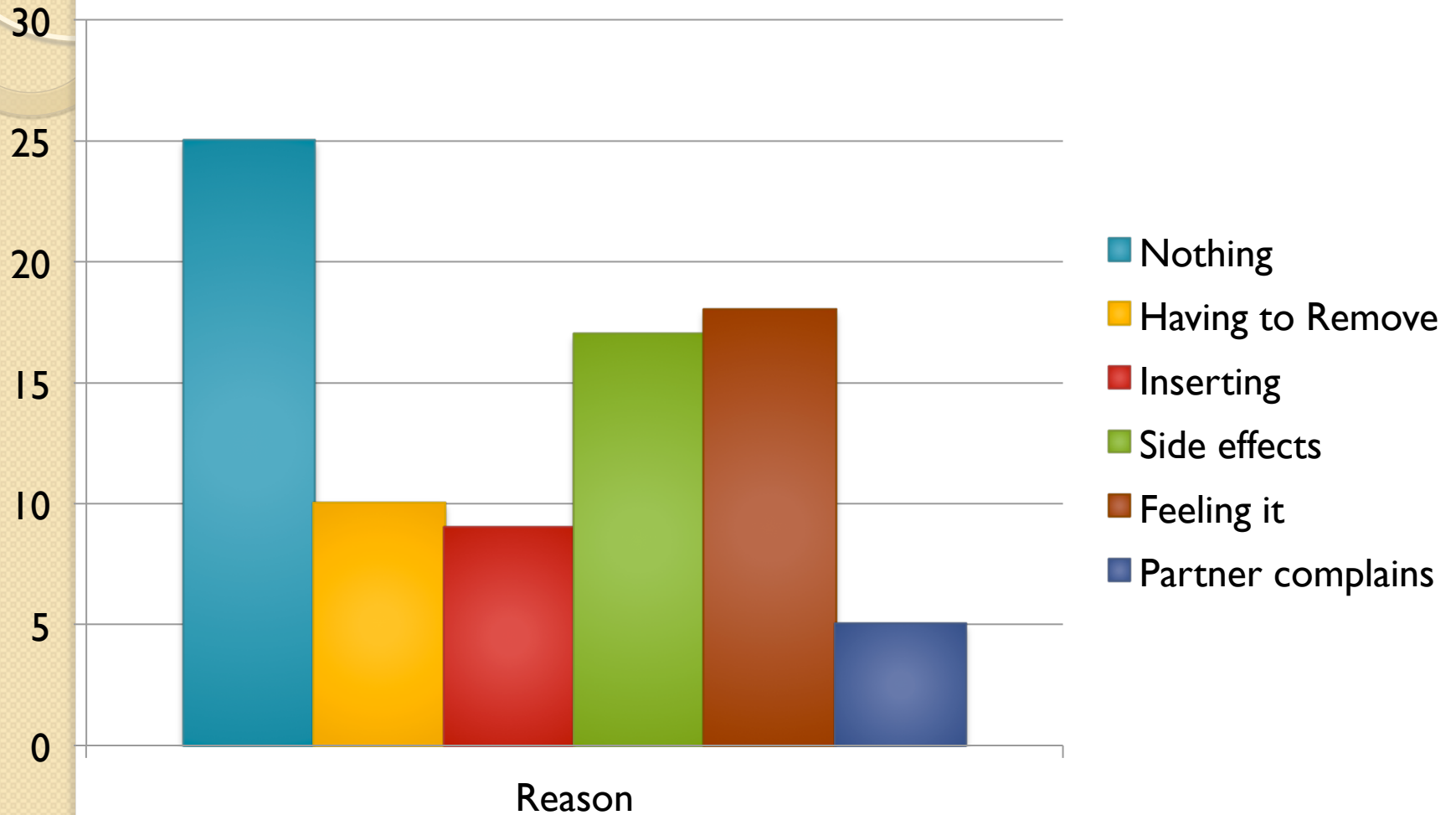


- Releases continuous dose of progesterone
- reinforces the inhibitory effect of breastfeeding on ovulation.
- Each ring used continuously for three months
- Rings can be used successively for up to one while breastfeeding

# CVR: What did you like the most?



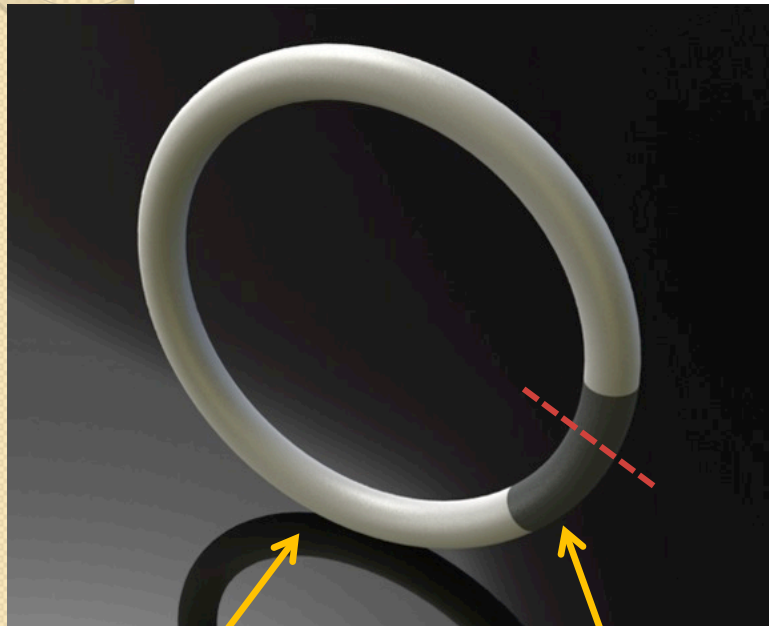
# CVR: What did you dislike the most?





# Multipurpose Prevention Technology

# TFV/Levonorgestrel (LNG) IVR: Segmented Reservoir Design



**TFV**

**LNG**

- Builds on the TFV-only reservoir IVR design
- Segmented approach allows for independent optimization of each drug's delivery needs
- LNG release rate is controlled by:
  - Rate-controlling membrane (thickness and diffusivity)
  - Length of the LNG segment