

Nuove sfide contraccettive per la donna di oggi



PAVIA 26/4/2015
ANNAMARIA MATTEI

Definition of Sexual Health



.....” **a state of physical, emotional, mental and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction or infirmity.**

Sexual health requires a positive and respectful approach to sexuality and sexual relationships, as well as **the possibility of having pleasurable and safe sexual experiences**, free of coercion, discrimination and violence.

For sexual health to be attained and maintained, the sexual rights of all persons must be respected, protected and fulfilled.”

WHO, 2006

What has remained the same

- Contraception is one of the most liberating interventions we have on offer for women.
- Contraception is good for women's health

Contracezione ormonale

Nel 1956 Pincus scopre l'associazione di un estrogeno con un progestinico (EP) che induce il blocco dell'ovulazione

Nasce così “la pillola” che segna una svolta rivoluzionaria nelle metodiche contraccettive



Il metodo viene considerato oggi il migliore avvicinandosi alle caratteristiche del contraccettivo ideale

quasi il 100% di efficacia
Indice di Pearl = 0,07-0,05

reversibilità

rischio inferiore
al 2%

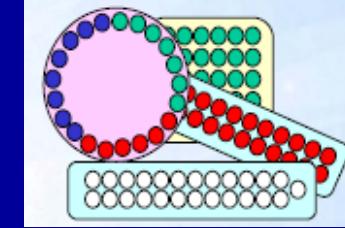
Requisiti necessari per un moderno contraccettivo

- **Alta efficacia contraccettiva**
- Quantità di ormoni più bassa possibile
- **Buon controllo del ciclo**
- Buona tollerabilità (compliance)
- Neutralità metabolica globale
- Buon bilanciamento fra componente estrogenica e progestinica

CONTRACCCEZIONE ORMONALE E BENESSERE

MIGLIORAMENTO:

- DELLA SALUTE GENERALE
- DELLA SALUTE RIPRODUTTIVA
- DEL BENESSERE GENERALE DEL SOGGETTO



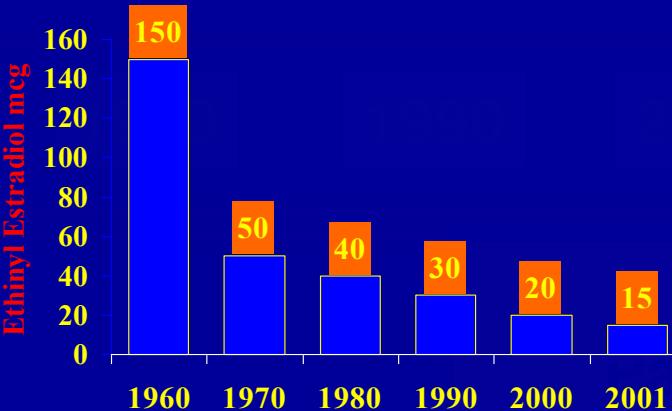
↑
COMPLIANCE

**EFFETTI
COLATERALI** ↓



1960

1970



Possibilità di formulazioni contenenti estrogeno naturale

Ricerca della giusta componente progestinica da associare

Nuovi regimi di somministrazione

acqua
contraccettiva

Incremento:

Tollerabilità
Sicurezza

↑
Compliance

2009

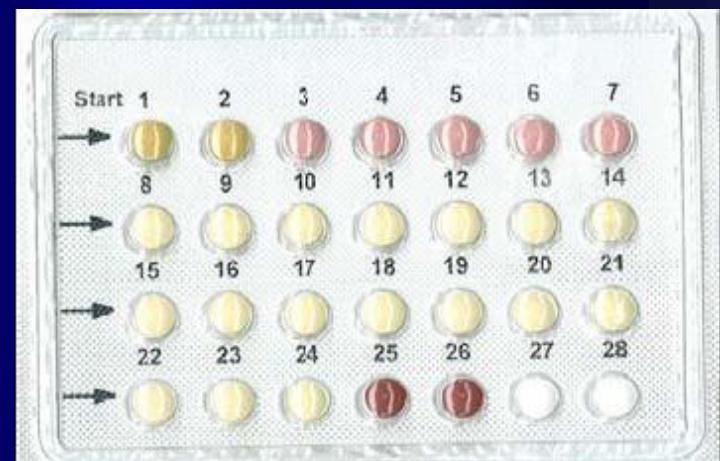
Novità nella contraccezione orale

uno sviluppo durato 15 anni !!



Fino ad oggi infatti, utilizzare l'estradiolo era risultato impossibile poiché non assicurava un sufficiente controllo del ciclo.

- **ESTROGENO NATURALE
(ESTRADIOLO VALERATO)**
- **PROGESTINICO I[^] Gen.
(DIENOGEST)**
- **REGIME DINAMICO DI
SOMMINISTRAZIONE
(A DOSAGGIO QUADRIFASICO)**





INDICE DI PEARL (IP)

Numero di gravidanze in 100 donne per 1 anno di utilizzo



18-35 aa	1.01
18-50 aa	0.79

Adjusted Pearl Index

18-35 aa	0.51
18-50 aa	0.421

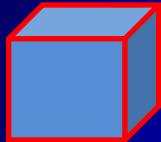
L'evoluzione componente estrogenica nella contraccezione EP

2011

Mestranolo

Etinilestradiolo : progressiva ↓ dosaggio
fino al limite necessario per ottimale risposta endometriale e per
adeguata estrogenizzazione (evitare rischio di osteopenia)

Valerato di estradiolo
in associazione quadrifasica con Dienogest



17 β estradiolo in associazione monofasica con
Nomegestrolo acetato

Estetrolo (E4) estrogeno di origine fetale con azione
antagonista su mammella

17 β estradiolo/ NomAC

Vantaggi:

**Riduzione del flusso abbondante,
non modifica dei parametri lipidici, glicidici e della coagulazione.**

Zoely è stato analizzato nell'ambito di due studi principali ai quali hanno partecipato 4 433 donne di età compresa tra i 18 e i 50 anni.

24 compresse attive bianche (1,5 mg di estradiolo e 2,5 mg di nomegestrolo acetato)
4 compresse inattive gialle.



INDICE DI PEARL (IP)
Numero di gravidanze in 100 donne
per 1 anno di utilizzo

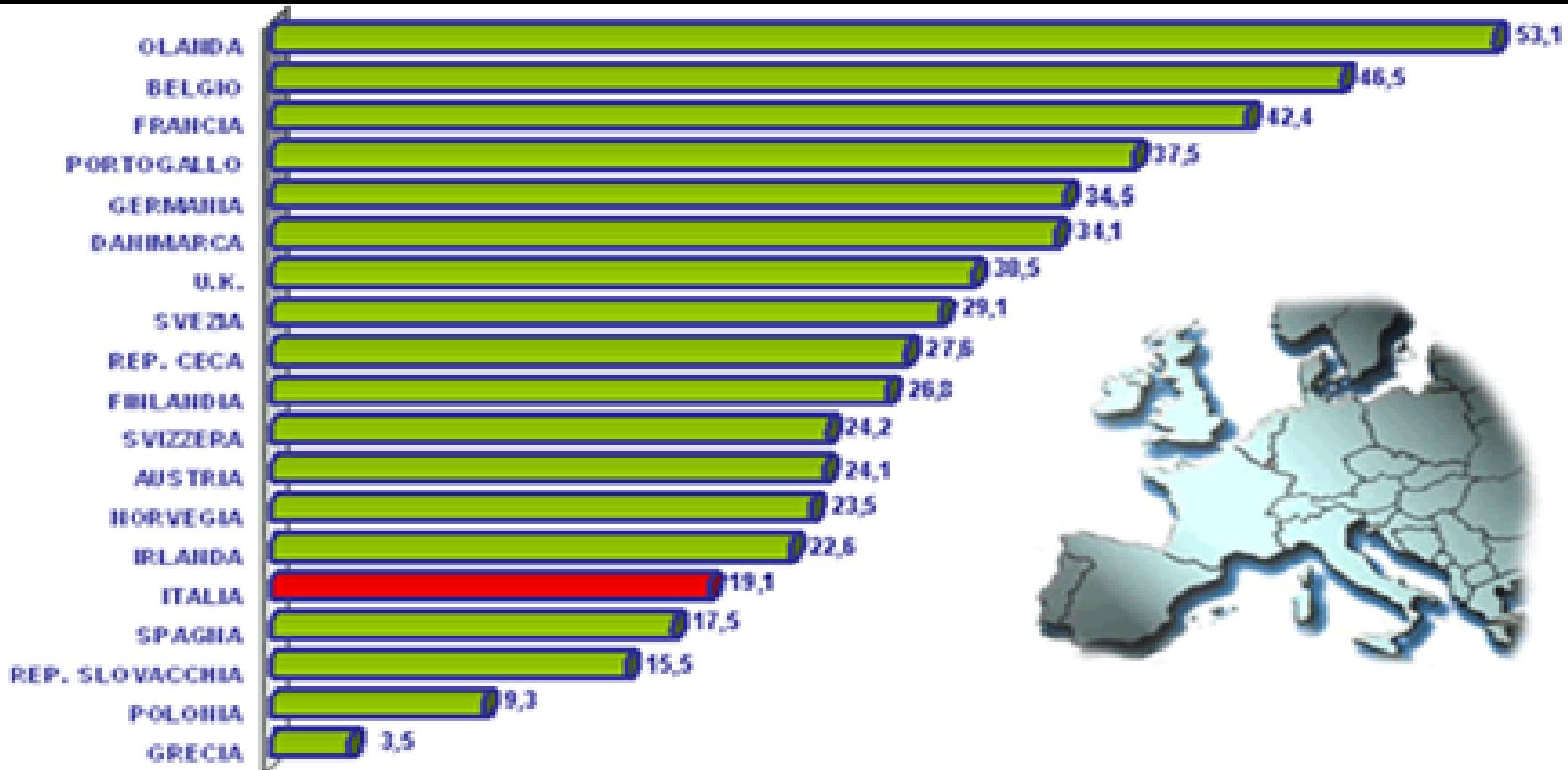


18-35 aa 1.2

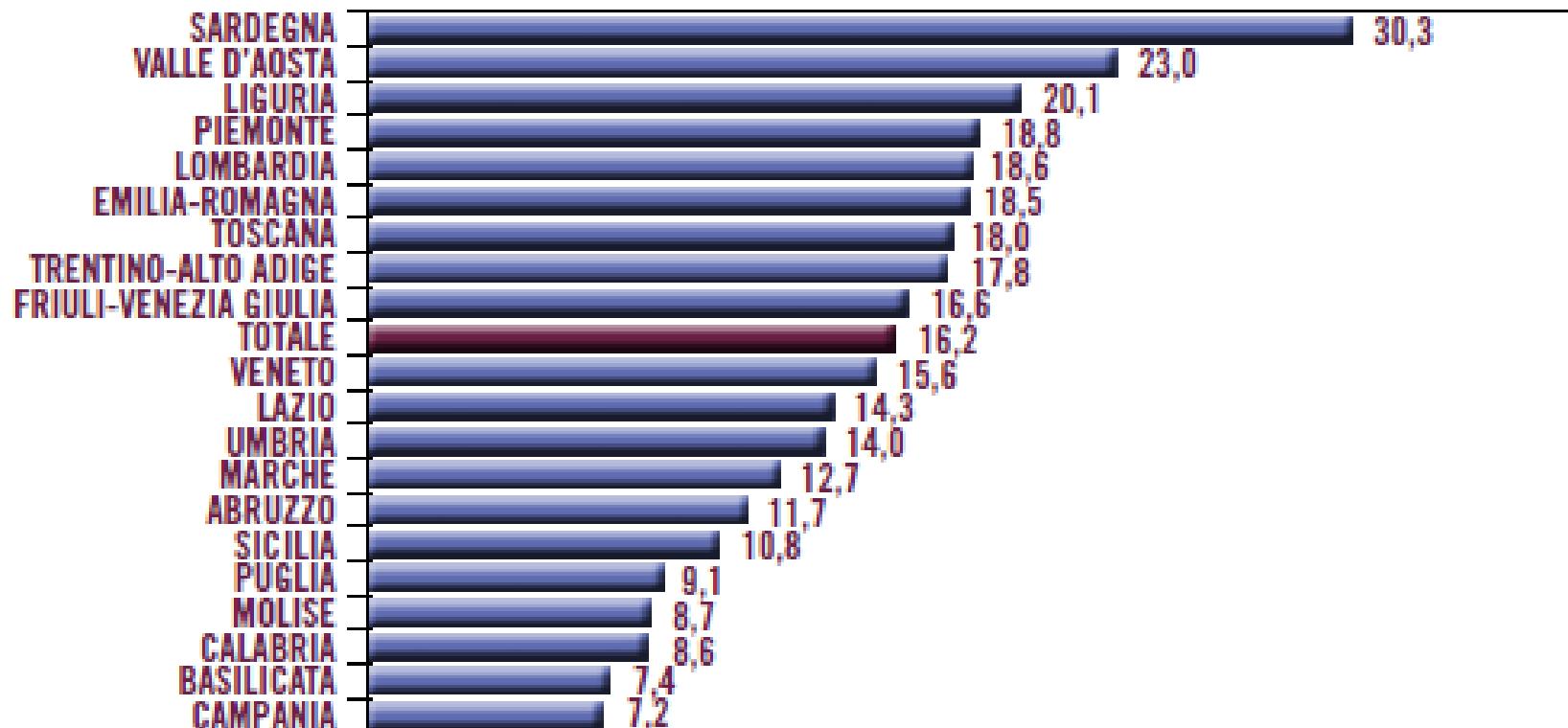
Adjusted Pearl Index

18-35 aa 0.4

Utilizzo CO in Europa



PERCENTUALE DI UTILIZZO DELLA PILLOLA CONTRACCETTIVA TRA LE DONNE ITALIANE, REGIONE PER REGIONE



Fonte ISTAT+IMF, aggiornata a giugno 2011

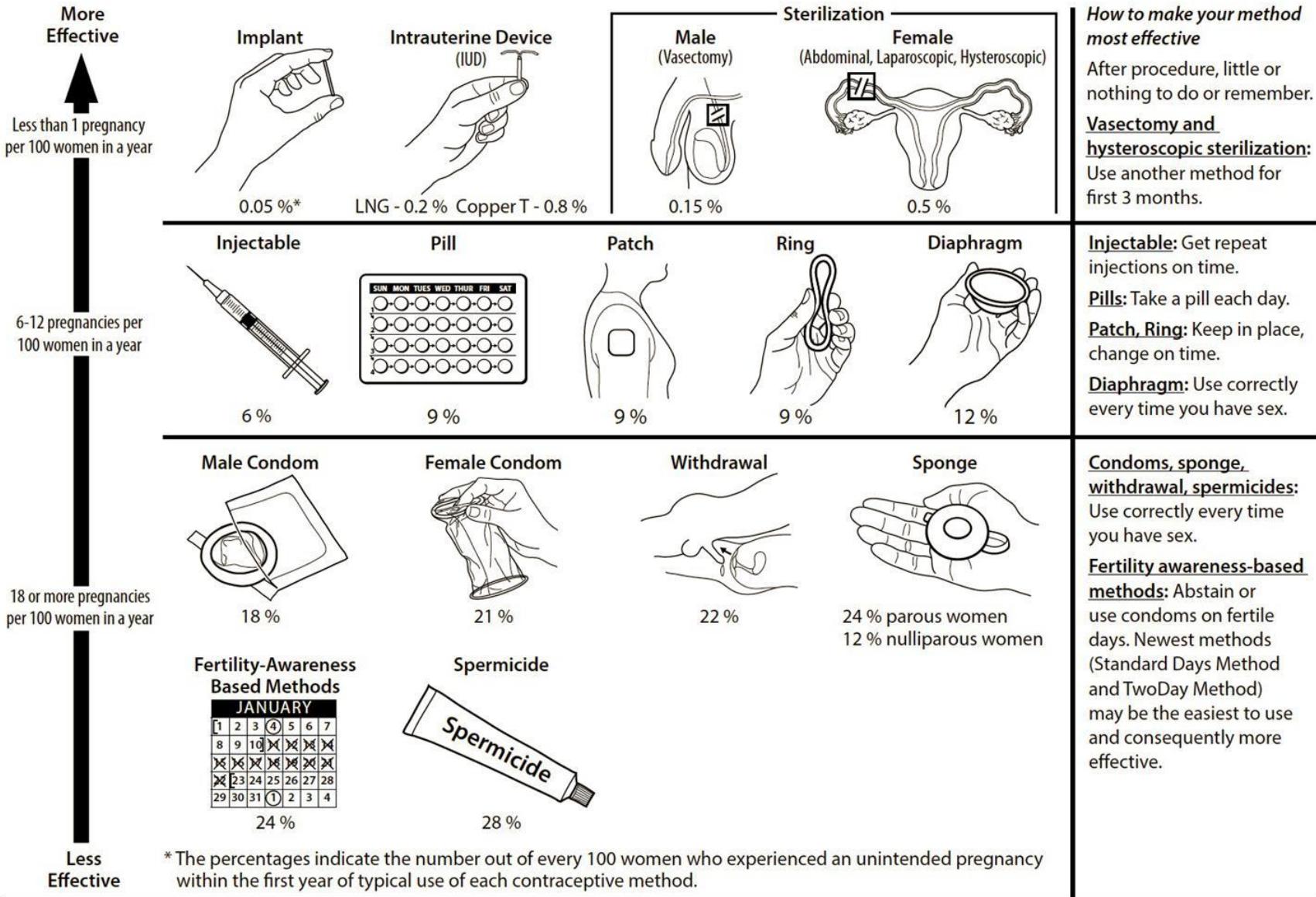
Siamo ancora lontani dagli standard europei..

- 59% delle donne dicono di aver dimenticato di prendere la pillola.
- 15% delle donne dicono di aver preso la pillola per non dover andare al ginecologo.
- 44% delle donne dicono di aver preso la pillola perché non hanno tempo per andare al ginecologo.

8 donne su 10 è capitato di dimenticare la pillola, il 30% ha paura che ciò accada, il 42% manifesta il timore di ingrassare o di avere problemi estetici, il 31% guarda con sospetto al suo doceoin ormonale¹. A molte donne pesa il fatto

Le donne italiane non rinunciano all'idea della contraccezione: desiderano però un contraccettivo che le faccia sentire libere (64%), sicure e tranquille (74%), ben tollerato e pratico da utilizzare (65%), che non rappresenti per loro un peso, un impegno, che non le faccia pensare, che consenta loro di dimenticarsi della contraccezione (71%).

Effectiveness of Contraceptive Methods



Il 40% delle giovani donne non usa contraccettivo

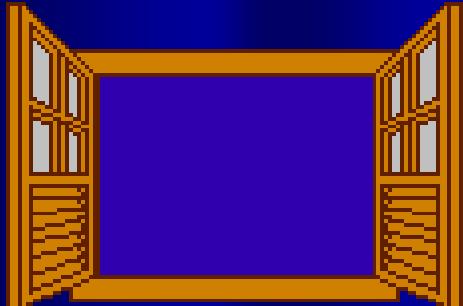
1 18% sceglie la pillola, ma 1 su 4 la dimentica una volta al mese

perfect use has a failure rate of 0.3% in the first year.

But in practice failure is much higher—closer to 8% or 9%.

1 Trussell J. Contraceptive failure in the United States. *Contraception* 2004;70:89-96.

2 Kost K, Singh S, Vaughan B, Trussell J, Bankole A. Estimates of contraceptive failure from the 2002 national survey of family growth. *Contraception* 2008;77:10-21.



Why LARC ??

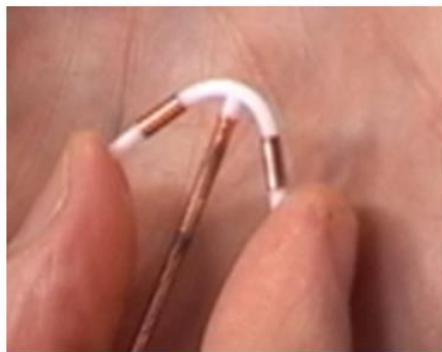
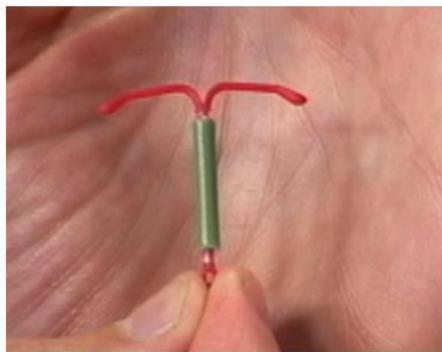
(Long acting reversible contraception)

LARC

- copper intrauterine devices
- progestogen-only intrauterine systems
- progestogen-only injectable contraceptives
- progestogen-only subdermal implants
- combined vaginal rings

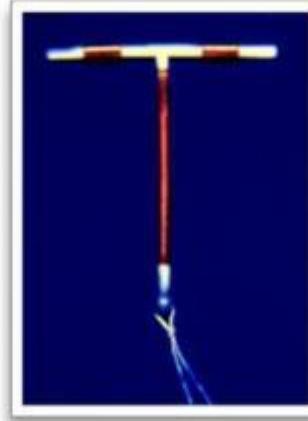
Types of LARCs

Generic	Brand	Reservoir	Duration
ENG implant	Nexplanon	68 mg ENG	Up to 3 years
LNG IUD 20 µg/24 h	Mirena	52 mg LNG	Up to 5 years
LNG IUD 13.5 mg	Jaydess	13.5 mg LNG	Up to 3 years
T380A Copper IUD	Copper T	380 mm ²	Up to 10 years



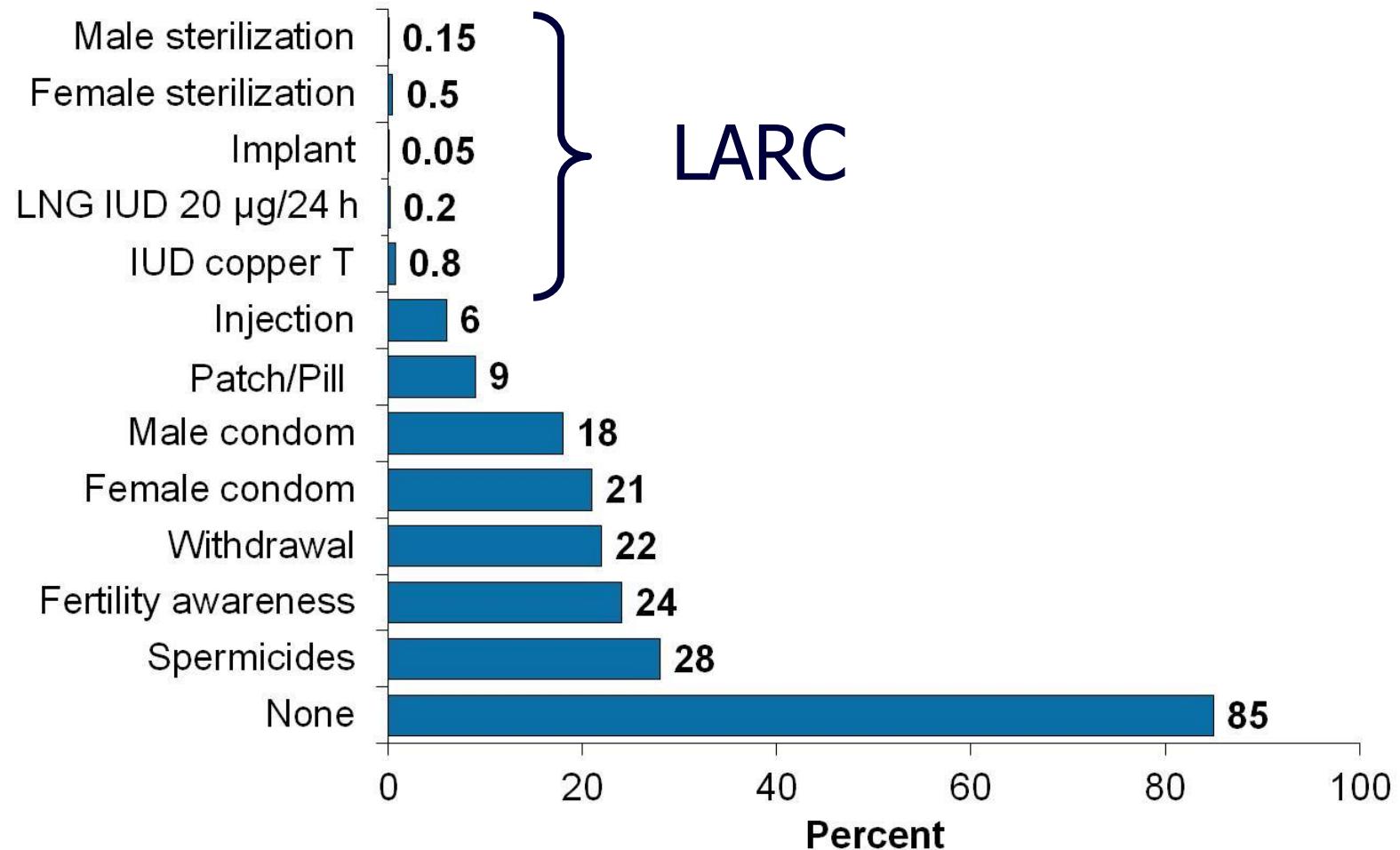
ENG = etonorgestrel; LNG = levonorgestrel.

Increased use of LARC*
**has the potential to lower unintended
pregnancy rates**



***LARC = Long-Acting Reversible Contraception**

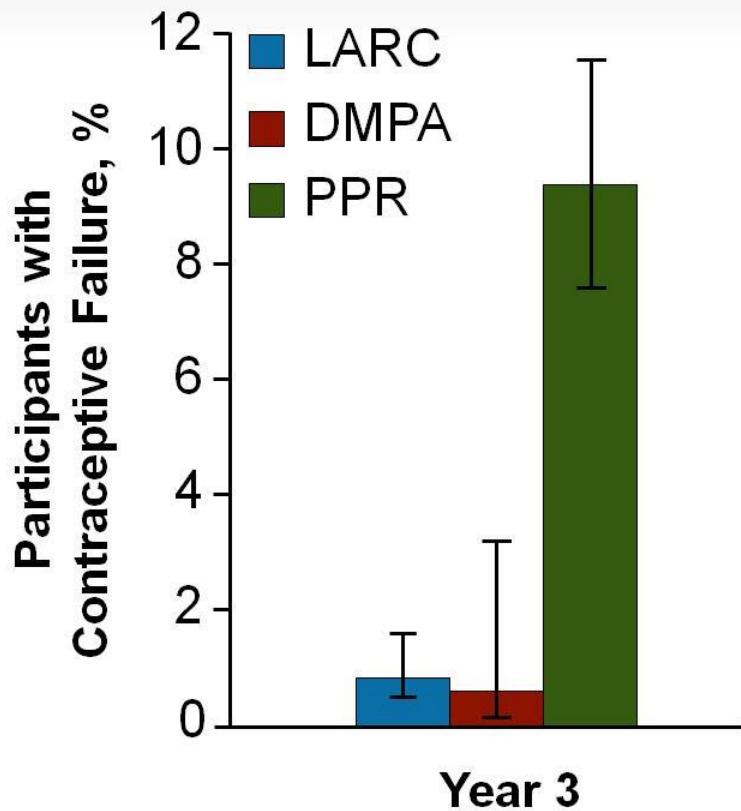
Unintended Pregnancy in First Year of Contraceptive Use (Typical Use)*



*From the 1995 and 2002 National Survey of Family Growth

Trussel J. Contraception. 2011;83:397-404.^[13]

CHOICE Study: Contraceptive Failure



The LARC methods were
22 times more effective
than pills, patch, or ring
(PPR)*

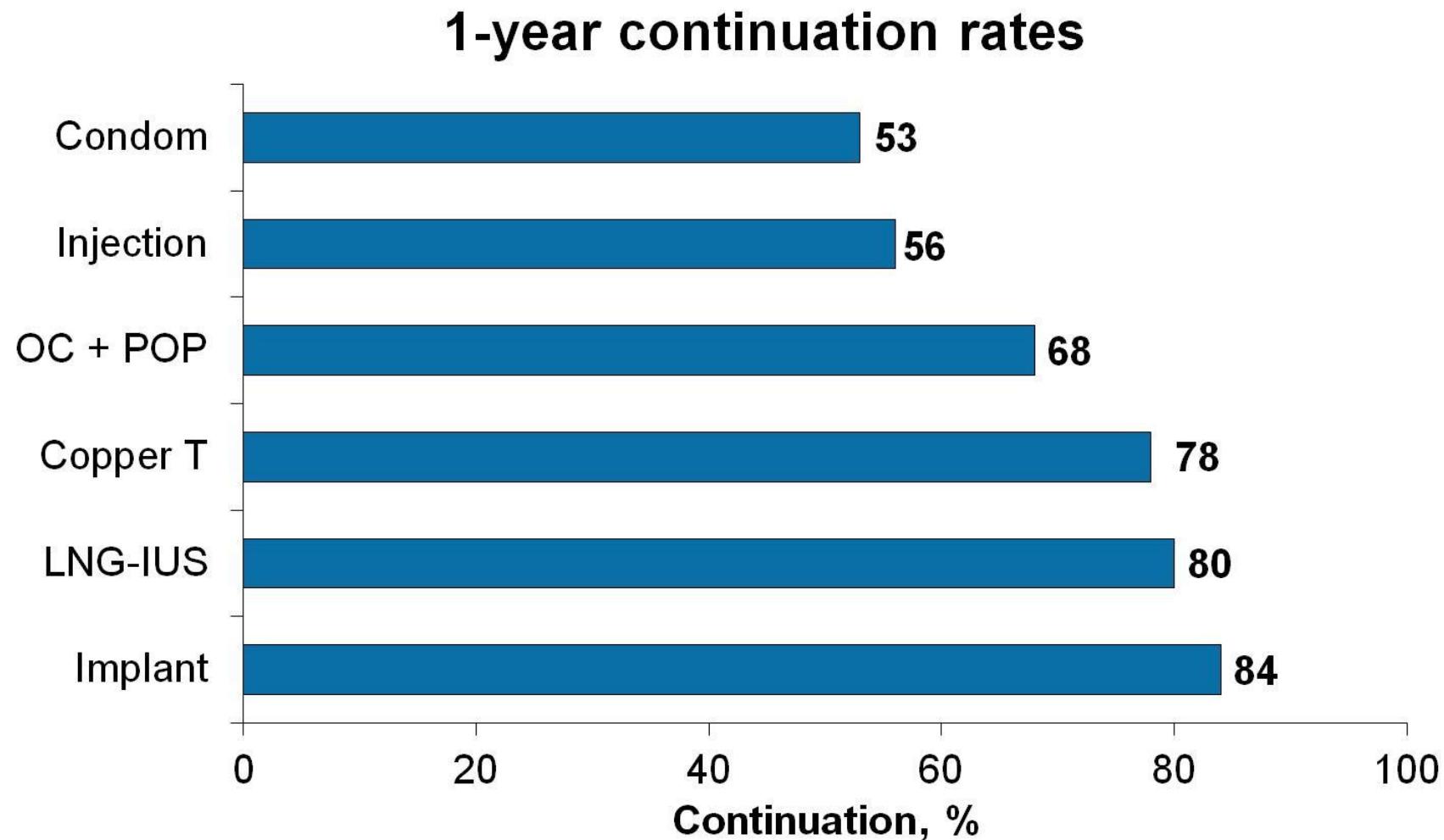
*Hazard ratio after adjustment for age, educational level, and history with respect to unintended pregnancy, 21.8; 95% confidence interval, 13.7 to 34.9; efficacy of DMPA injection was similar to LARC, but failures for DMPA were counted only in users who returned for injections, so this failure rate was underestimated.

- Teenage pregnancy rates have fallen to their lowest levels since record began
- The use of LARC has increased : 28% from community contraception-service users in 2012/13 from 18% in 2003/2004

but

- Up to 50% of pregnancies are still unplanned
- Condom and pill remain the most popular method of contraception

LARC Continuation Rates Are the Highest of All Reversible Methods



Who Are Appropriate Candidates for LARCs?

- Just about every woman of reproductive age who seeks very effective, convenient, safe, and reversible contraception
- Long acting refers to 1 year or longer
- Very few contraindications
- Candidates include:
 - Adolescents
 - Nulliparous women
 - Patients with contraindications to estrogens

WHO Medical Eligibility Criteria, Classification Categories

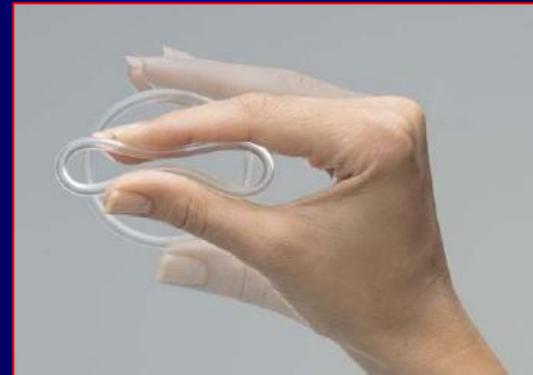
Classification Category	With Clinical Judgment	With Limited Clinical Judgment
1	No restriction: Use method in any circumstances	Yes Use the method
2	Generally use: benefits generally outweigh risks	Yes Use the method
3	Generally do not use: risks outweigh benefits	No Do not use the method
4	Unacceptable health risk: method not to be used	No Do not use the method

WHO Medical eligibility criteria for contraceptive use. 4th ed, 2009.

Few Absolute Contraindications to LARCs (US MEC 4)

- Pregnancy
- Unexplained vaginal bleeding
- Sepsis (postabortion or puerperal)
- Acute cervicitis or PID
- Breast cancer in last 5 years (especially hormonal LARCs)
- Uterine distortions or fibroids that interfere with placement of IUDs
- Wilson disease (do not use copper IUD)

NUVARING



Not properly a LARC but a very good alternative way of delivering combined EE & Progestogen



Nuva Ring

● Vaginal Ring

- 15µg/day EE and 120µg/day Etonogestrel
- Flexible transparent ring, 4mm thick x 54mm diameter
- Latex free

● Use

- 1 Ring for 3 weeks then 7 day break
- Can be used with tampons and during SI

● Pharmacology

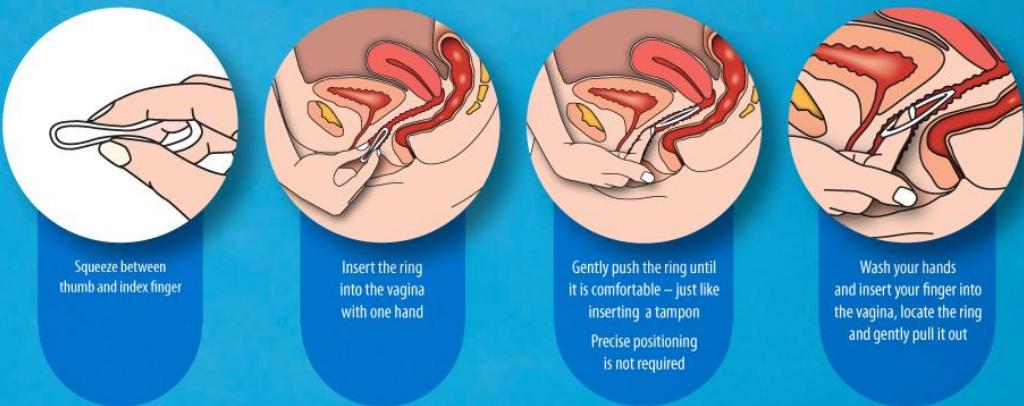
- Avoids first pass metabolism & GI interference with absorption
- Systemic EE is 50% of that of 30 µg EE COCP

● Efficacy

- Pearl Index 0.64 (perfect use)
- Comparable to COCP

NuvaRing is simple to insert

- Unimportant where NuvaRing sits within the vagina as it is held in place by the vaginal wall
- Expulsion is rare; 0.5% incidence seen in 3,333 women over 33,462 cycles¹
- Imperceptible to most women (and their partners)²



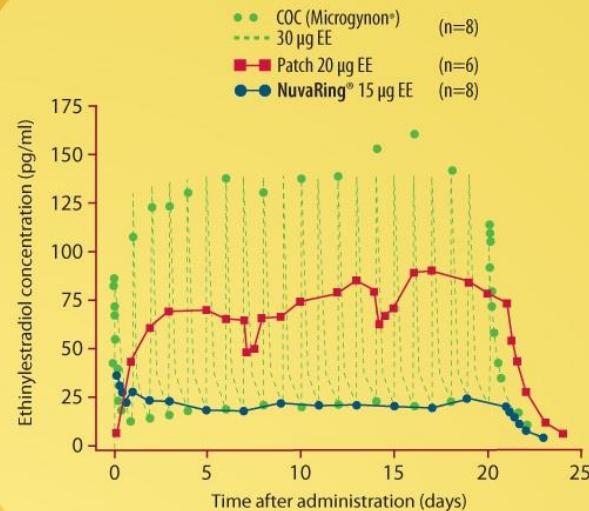
References:

1. Kaptein M and Zampaglione E. Poster presented at Annual meeting of American College of Obstetricians and Gynecologists, San Francisco May 7-11 2005.
2. Novak A et al. Contraception 2003;67:187-194.

NUVARING®
(etonogestrel/ethynodiol Ring)

Combined contraception at the lowest effective daily dose¹

- NuvaRing provides low, steady and continuous delivery of hormones, resulting in stable serum concentrations¹
- More constant hormone delivery than achieved with contraceptive patch or oral combined pill¹



Adapted from van den Heuvel



Reference:

1. van den Heuvel MW et al. Contraception 2005 Sep; 72(3): 168-174.

NUVARING®
(etonogestrel/ethinylestradiol) Ring

Nuva Ring

- Compliance
 - >85% of cycles compliant in trials
- Acceptability
 - Low incidence of Break through bleeding
 - Better than COCP for cycle control
 - >90% trial subjects found easy to insert and remove
- Safety
 - Same metabolic and coagulation effects as most combined methods
- Storage
 - 2-8°C before dispensing to patient
- Cost: could be a problem

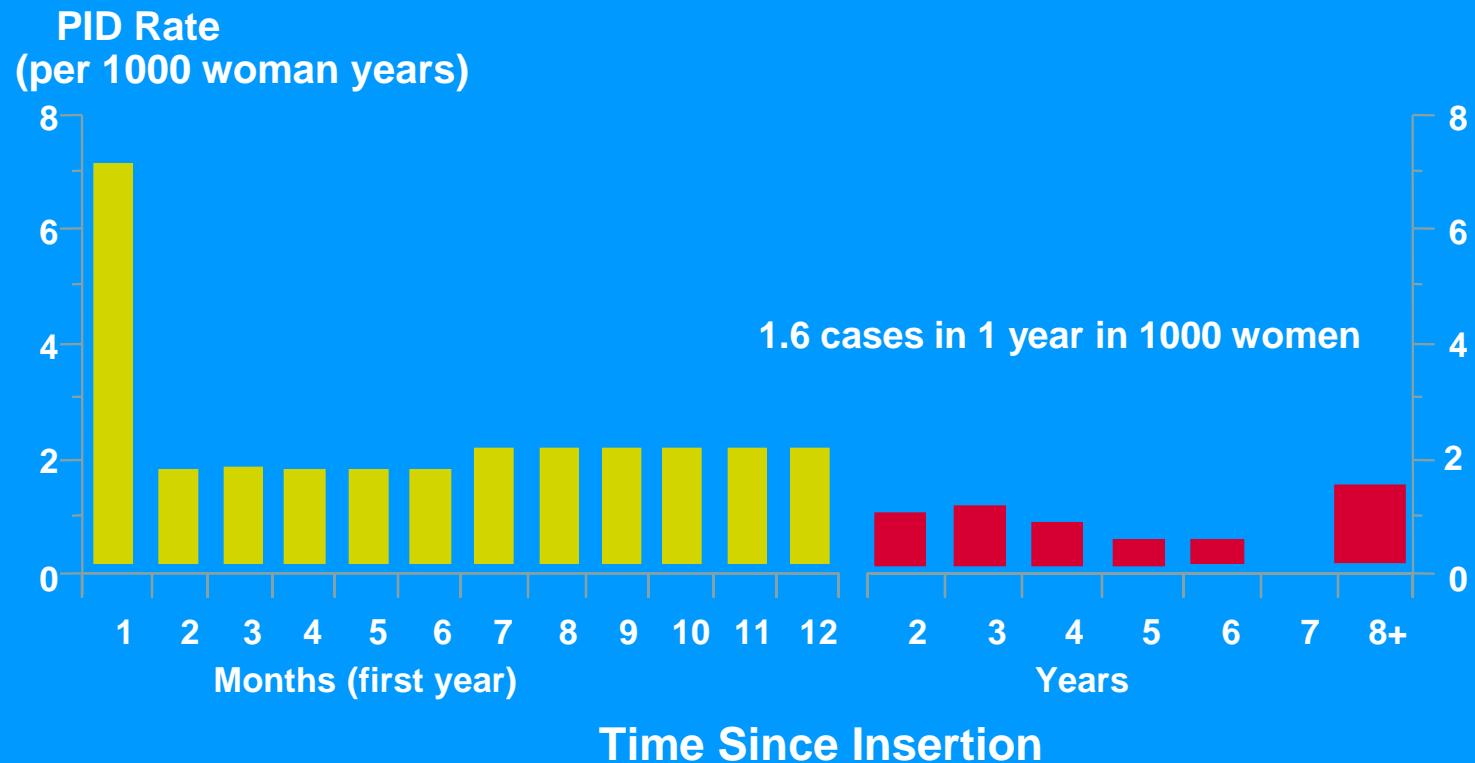
Myth and Misconception

IUD - IUS



Risk of PID: Very Low and Far Lower Than Many Providers Erroneously Believe

PID Incidence Rate by Time Since Insertion



Source: Farley et al, 1992, in FHI 2004

Insertion Protocols

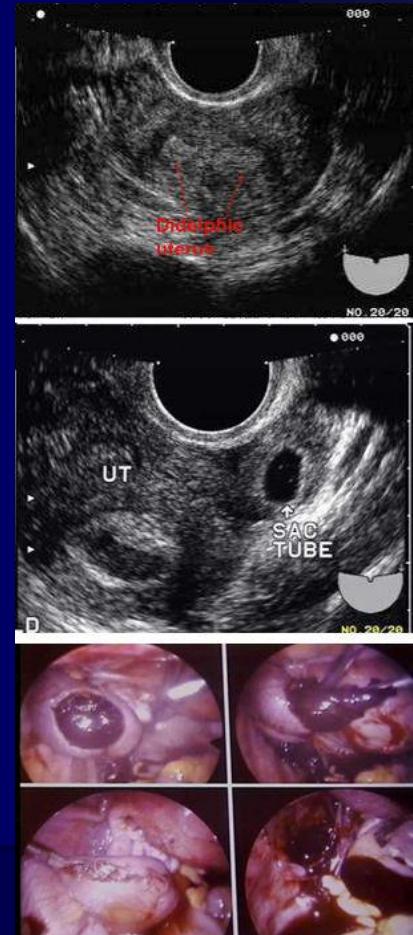
- Treat mucopurulent discharge or known STI before insertion
- Routine antibiotic prophylaxis is not recommended before insertion

IUDs Do Not Cause Infertility

- Infertility is not more likely after IUD discontinuation compared to other reversible methods
- No evidence that IUD use is associated with subsequent infertility
- Chlamydia, not previous IUD use, is associated with infertility

IUD/IUS and Ectopic pregnancy

- Incidence of ectopic pregnancy 0.02 per 100 woman years.
- This represents an 80-90% reduction in risk compared with women not using contraception.
- **Between 5-50% of conceptions with the LNG IUS are ectopic.**





THE AMERICAN COLLEGE OF
OBSTETRICIANS AND GYNECOLOGISTS

Office of Communications
tel: 202-484-3321
communications@acog.org
www.acog.org

IUDs and Contraceptive Implants Safe for Teens

September 20, 2012

Washington, DC -- Implants and intrauterine devices (IUDs) should be offered as first-line contraceptive options for sexually active adolescents, according to new guidelines issued today by The American College of Obstetricians and Gynecologists (The College). Both the implant and the IUD are the most effective reversible contraceptives for preventing unintended pregnancy and abortion in teens and adult women.

Insertion

- Little evidence to suggest that IUD insertion is more technically difficult in adolescents
- More than one half of nulliparous women will report discomfort with placement
- Provide anticipatory guidance regarding pain before insertion

Complications are Uncommon

- Expulsion rate: 5–22% among adolescents
- Perforation: 1 per 1,000 insertions or fewer

Managing Bleeding Concerns

- Provide anticipatory guidance
- Evaluation of abnormal bleeding similar to non-IUD users



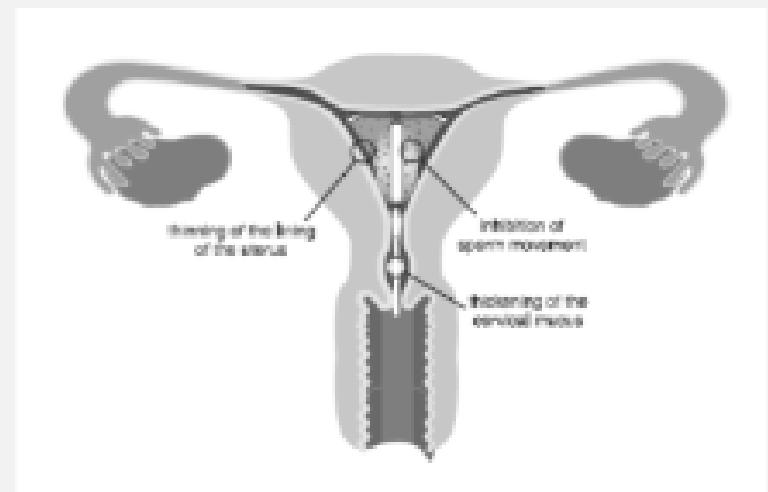
IUS

So what is Mirena?

- An T-shaped intrauterine device that contains 52 mg of levonorgestrel in its stem
- Releases 14 ug/day over 5 years
- This is equivalent to taking a Microlut (minipill) every second or third day
- But the hormone is concentrated within the uterus & serum levels are 4 times lower than after oral ingestion

LNG IUS MECHANISMS OF ACTION

- Thickens cervical mucus
- Inhibits sperm function in uterus
- Reduces monthly growth of the lining of the uterus making periods lighter and shorter; there is no evidence that LNG IUS has any impact on implantation
- LNG IUS can also lessen menstrual blood loss in women who have heavy menstrual flow

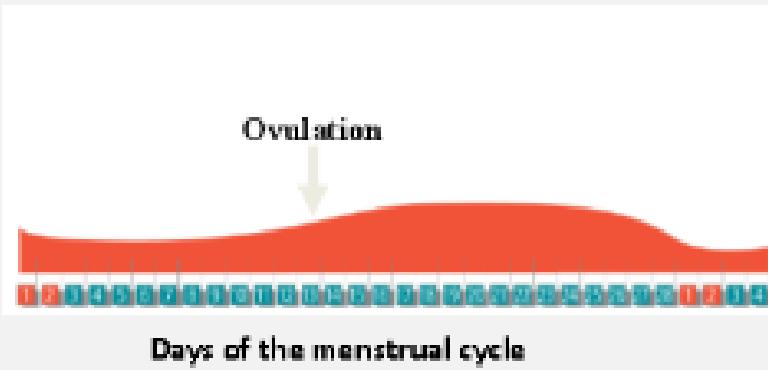
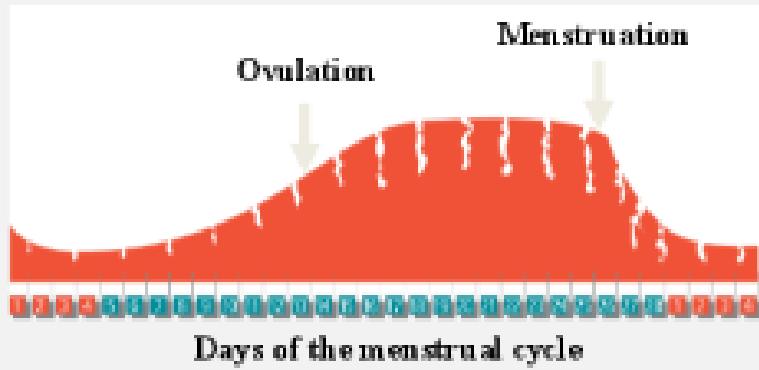
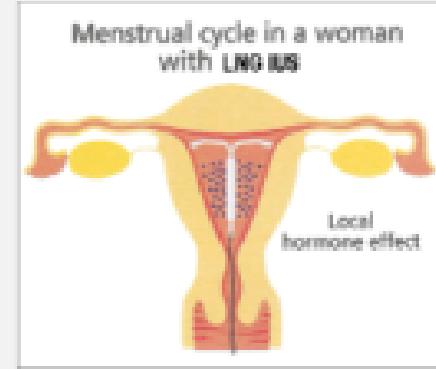
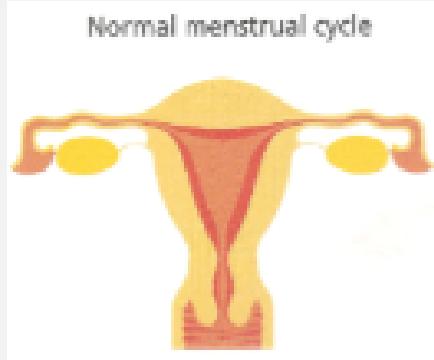


Source: Mirena prescribing information March 22, 2011

Menstrual Effects: LNG IUS

- Bleeding duration and amount decreases initially and over time
- 70% experience oligomenorrhea or amenorrhea within 2 years of insertion

LNG IUS ENDOMETRIAL EFFECTS



(: LNG IUS) should be a first-line option for the dual purposes of)



MENORRHAGIA

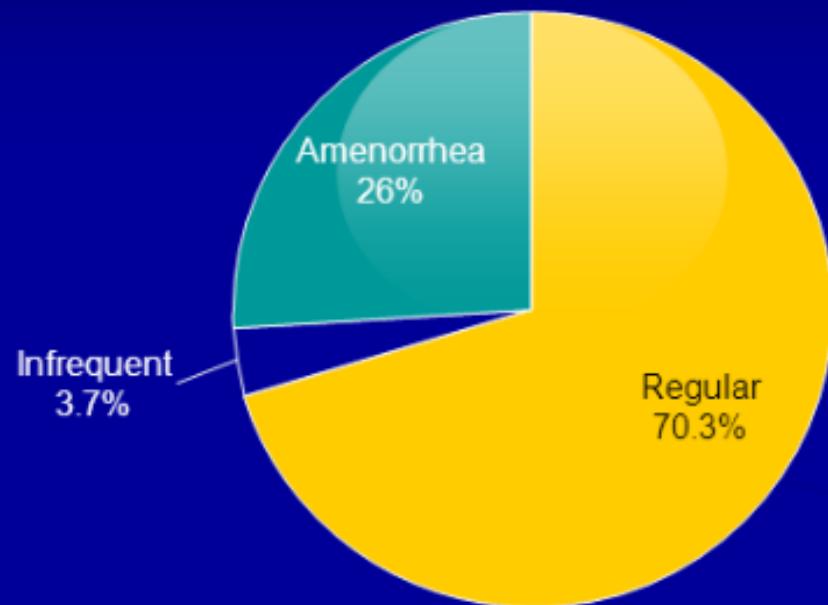
CONTRACEPTION



①

③

Bleeding pattern in the first 5-year period



Rönnerdag M, Odland V. Acta Obstet Gynecol Scand 1999;78:716-21

Intrauterine System Provides Long-Term Relief of Endometriosis Pain



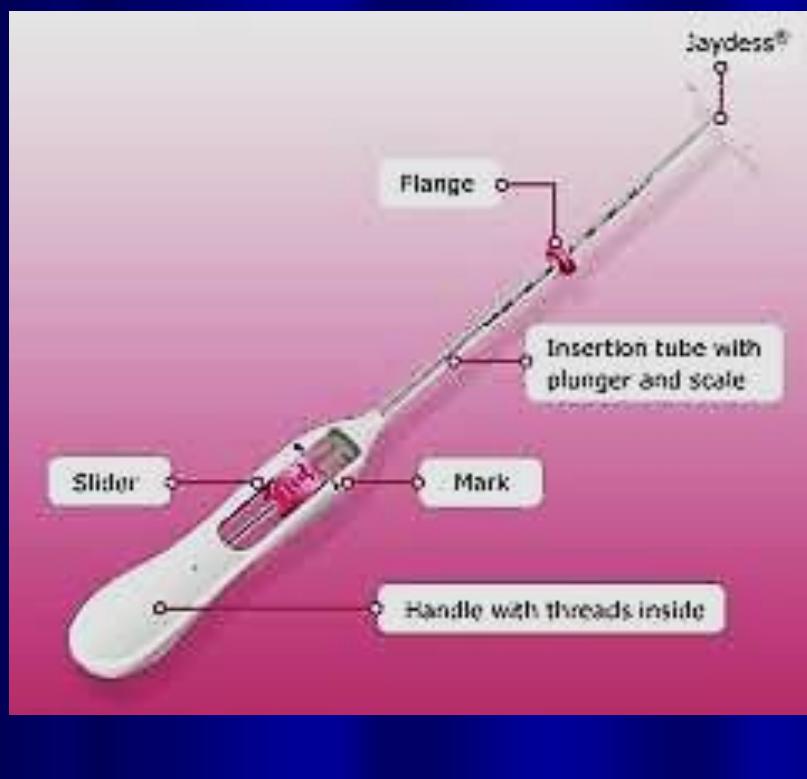
Obstet Gynecol 2012;119:519-526.

Who cannot use a Mirena?

- Absolute contraindications:
 - Pregnancy
 - Active PID
 - Undiagnosed abnormal uterine bleeding
 - Liver tumour
- Relative contraindications:
 - Nulliparity
 - Within 6 weeks of term pregnancy
 - Cervicitis, history of ectopic or PID
 - Congenital or acquired uterine abnormality
- Lactation OK – only 0.1% of the Levonorgestrel goes into breast milk

What is new – IUS Jaydess®

www.fsrh.org/pdfs/CEUProductReviewJaydess.pdf



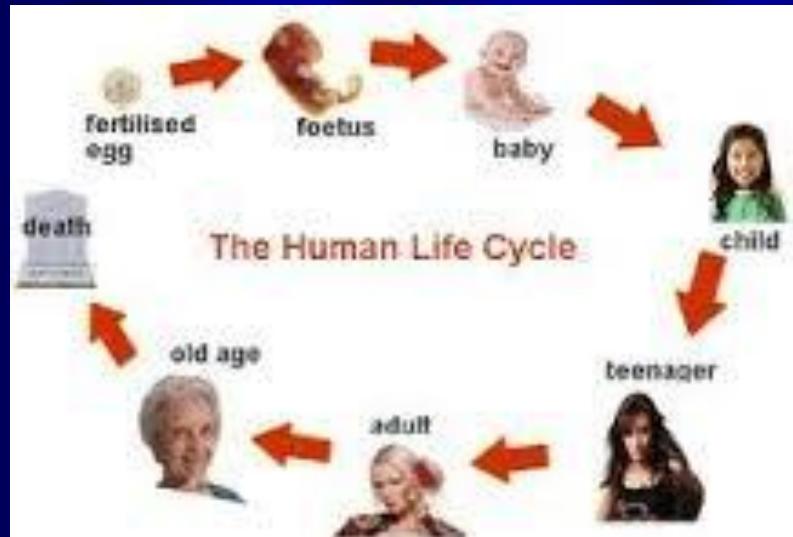
What is new – IUS Jaydess®

	Jaydess®	Mirena®
Insertion tube diameter	3.80mm	4.40mm
Duration of use	3 years	5 years
Dose	13.5mg	52mg
Indications	Contraception	Contraception Idiopathic menorrhagia Endometrial protection in HRT

What is new – IUS Jaydess®

- Women using Jaydess are less likely to experience amenorrhoea
- Jaydess contains a silver ring which distinguishes it from other intrauterine devices on ultrasound scan or x-ray
- The safety and efficacy of Jaydess have not been studied in women aged below 18 years
- The Summary of Product Characteristics (SPC) for Jaydess states that it is not first choice for contraception in nulliparous women as clinical experience is limited

Choices of Contraception in the different stages of reproductive life



Puberty to first sexual intercourse

First sexual intercourse until childbirth

Perimenopausal

Spacing pregnancies after breast feeding

During breast feeding

Completed family

UKMEC guidance for LARC use according to age



UKMEC guidance

- Depo – menarche to < 18 yrs = 2
18 to 45 yrs = 1
>45 yrs = 2
- Nexplanon - menarche to >45 yrs = 1
- IUD – menarche to < 20 yrs = 2
> 20 yrs = 1
- IUS (Mirena-Jaydess) –
- menarche to < 20 yrs = 2
> 20 yrs = 1



Special Populations

Adolescents^a

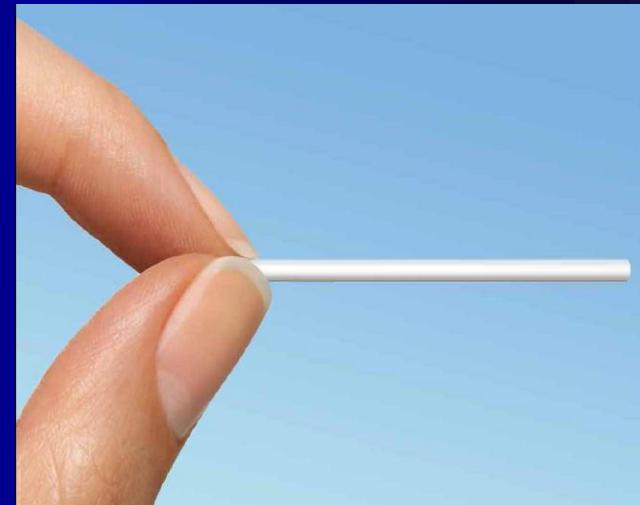
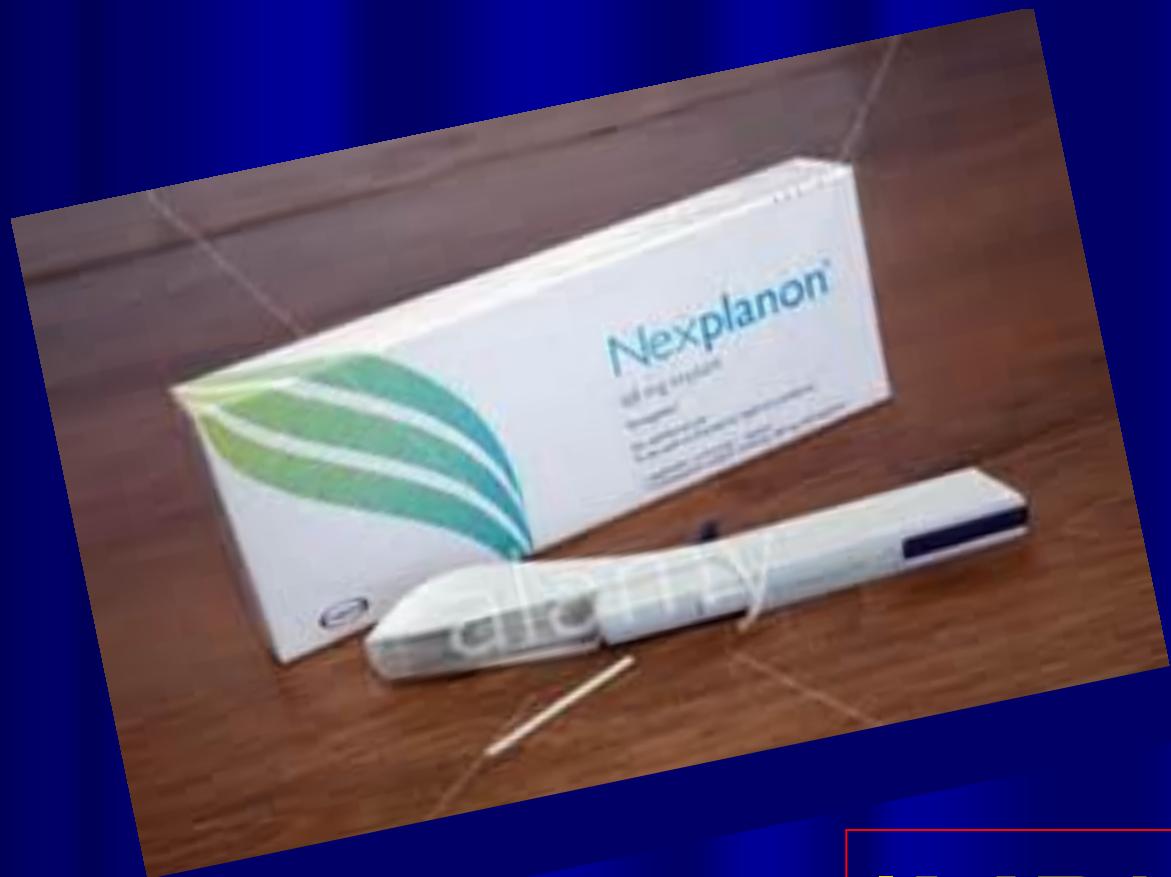
- Complications rare and differ little from those in older women
- Can be inserted without technical difficulty

Nulliparous women^{b,c}

- Can safely use available IUDs

Pain and anxiety^d

a. ACOG. *Obstet Gynecol.* 2009;114:1434^[11]; b. Hubacher D, et al. *Contraception.* 2007;75:S8-11^[18]; c. Nelson A, et al. *Obstet Gynecol.* 2013;122:1205-1213^[19]; d. Hillard PJ. *J Adolesc Health.* 52(Suppl 4):S40-S46.^[20]



IMPLANT

The Single-Rod Contraceptive Implant

- Most effective method of reversible contraception
- Etonogestrel (68 mg)
- Discreet
- Rapidly reversible
- Approved for use up to 3 years

Short Insertion and Removal Time

Insertion

< 1 minute



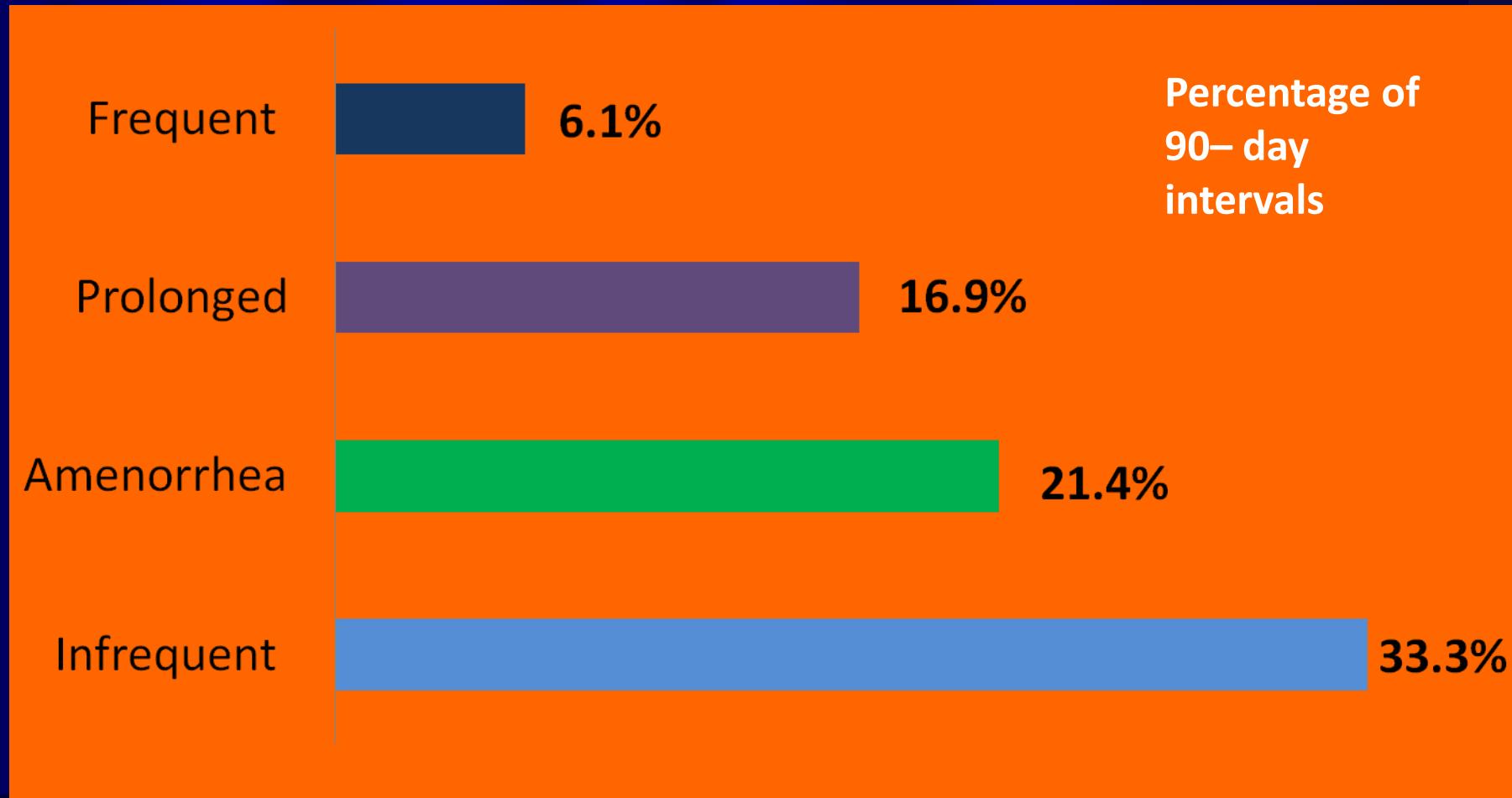
Removal

< 3 minutes



Bleeding Patterns with Implant

First 2 Years



Darney P, Patel A, Rosen K, Shapiro LS, Kaunitz AM. Safety and efficacy of a single-rod etonogestrel implant (Implanon): results from 11 international clinical trials. Fertil Steril 2009;91:1646–53

Bleeding Patterns Summary

- Provide anticipatory guidance
- Favorable bleeding patterns experienced in the first 3 months are likely to continue
- Unfavorable patterns have a 50% chance of improving
- Women with low body weight have fewer bleeding and spotting days

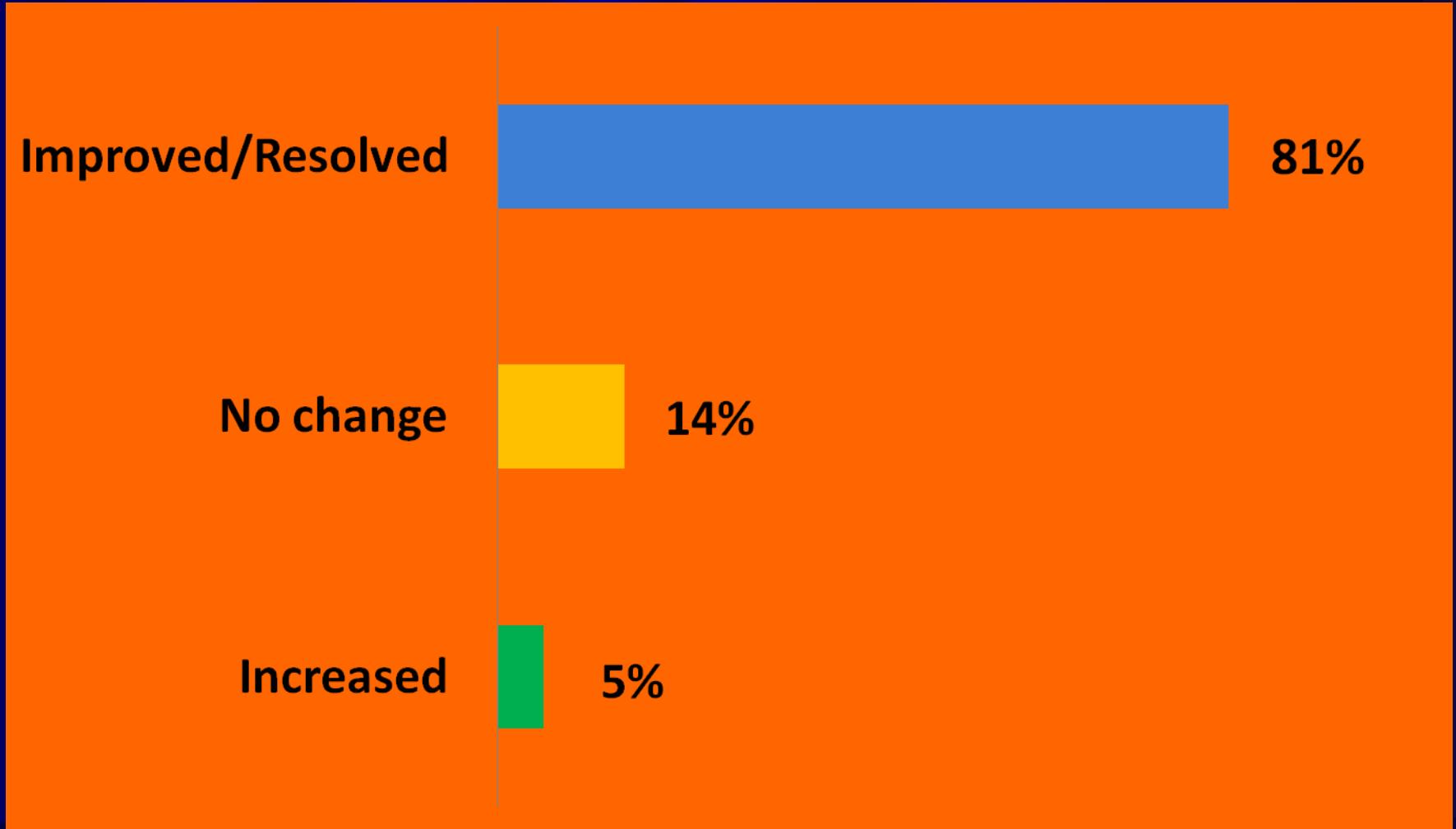
Weight Gain

- 6–12% of users report weight gain
- Only 2.3% discontinue due to weight gain



Darney P, Patel A, Rosen K, Shapiro LS, Kaunitz AM. Safety and efficacy of a single-rod etonogestrel implant (Implanon): results from 11 international clinical trials. Fertil Steril 2009;91:1646–53

Non-Contraceptive Benefit: Dysmenorrhea Improvement



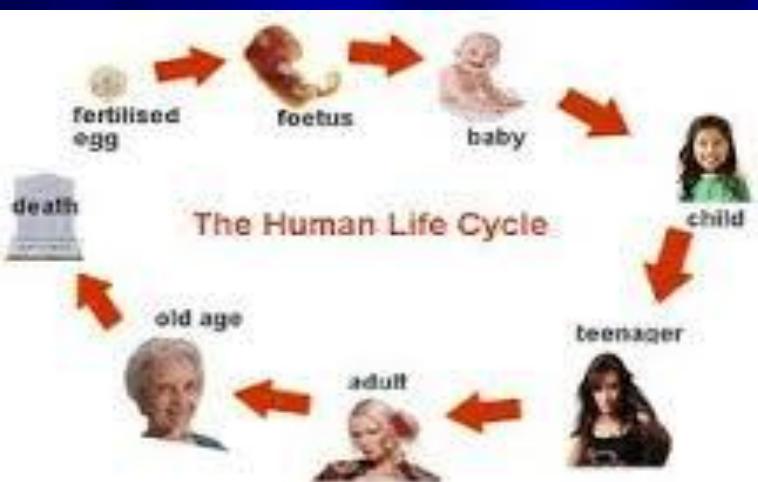
Shokeir T, Amr M, Abdelshaheed M. The efficacy of Implanon for the treatment of chronic pelvic pain associated with pelvic congestion: 1-year randomized controlled pilot study. Arch Gynecol Obstet 2009;280:437–43

Method Match Comparison Chart



Effectiveness	Extremely Effective (99%)	Extremely Effective (99%)	Extremely Effective (99%)	Very Effective (92%)
Requires healthcare provider visit	Yes	Yes	Yes	Yes
Timing of use or replacement	Effective for 10-12 years	Effective for 5-7 years	Effective for 3 years	Replace monthly
Protection from STDs/STIs	No	No	No	No
Quickly reversible	Yes	Yes	Yes	Yes
Private (not detectable by partner)	Yes	Yes	Yes	No
Possible side effects	▶ Heavier periods, increased...	▶ Irregular or no...	▶ Irregular or no...	▶ Nausea, headaches, breast...

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Choices of Contraception in the different stages of reproductive life



Puberty to first sexual intercourse

- Contraception used for its non-contraceptive benefits
- Sex Education:
promoting the possibility of having pleasurable and safe sexual experiences

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Full choices

IUD/IUS **can** be fitted if nulliparous
Depo – fertility return time variable
If adolescent – remember Depo and bone density
Remember safe sex message



Breastfeeding

- All LARC methods could be used if no contraindications
- Depo = UKMEC 2 if <6 weeks postpartum
- IUD / IUS = UKMEC 3 if 48 hours postpartum
- CHC contraindicated
- Lactational amenorrhoea – if exclusively breast feeding including night time feeds – 98% effective

Choices of Contraception in the different stages of reproductive life

Perimenopause

- Still need for contraception
- HRT is not contraceptive
- IUS may be used as part of HRT regime – endometrial protection, licensed for 4 years use
- Stop Depo at age 50 yrs – risk of osteoporosis
- Nexplanon/IUS – use FSH to determine when to stop contraception
- Safer sex message – increase in incidence of STI in divorced, newly single older people



Long-acting reversible contraception

National Institute for Clinical Health and Excellence (NICE) 2005

- Women should be offered a choice of all methods including LARC.
- All LARC methods are more cost effective than the combined oral contraceptive pill even at 1 year of use.
- IUDs, IUS and implants are more cost effective than the injectable contraceptives.
- Increasing the use of LARC will reduce unwanted pregnancies

Factors influencing the provision of long-acting reversible contraception in California.
Biggs MA, Harper CC, Malvin J, Brindis CD.
Obstet Gynecol 2014 Mar;123:593-602.

Indagine sulle opinioni e la pratica dei metodi LARC tra i professionisti di 639 strutture pubbliche con servizio di pianificazione familiare

Nonostante i progressi significativi sull'accesso ai metodi LARC, molti clinici conservano convinzioni che limitano l'utilizzo degli IUD e non hanno sufficienti conoscenze sugli impianti.

Ciò suggerisce la necessità di formazione e di aggiornamento sui recenti sviluppi delle raccomandazioni all'utilizzo