Contraceptive Update 2014: Improving use and prevention of unintended pregnancy

Larry Leeman MD MPH
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Disclosures

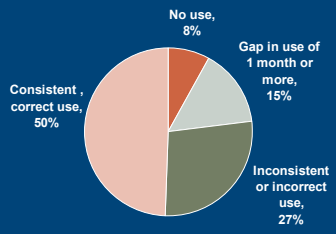
- No financial conflicts of interest
- Some slides of from ARHP (Association of Reproductive Health Professional)
- arhp.org and Alan Guttmacher Institute www.guttmacher.org/

Objectives

Participants will understand:

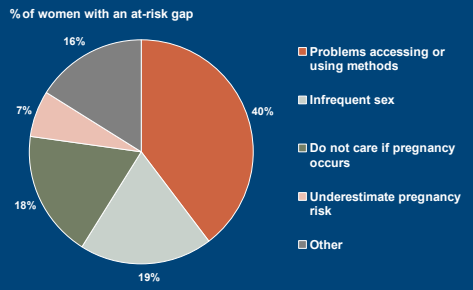
- Epidemiology of contraceptive failure and unintended pregnancy
- Choice study findings that Long Acting Reversible Contraceptives have superior efficacy
- Use of postpartum contraception
- Techniques to increase success of emergency contraception

Half of women at risk are not fully protected from unintended pregnancy

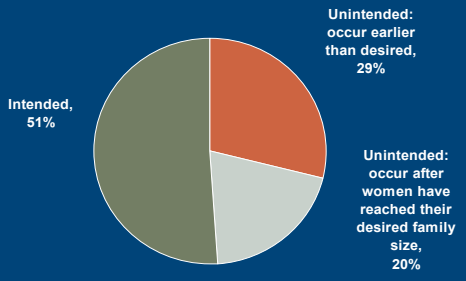


28 million adult women at risk for unintended pregnancy

Women report a variety of reasons for contraceptive nonuse

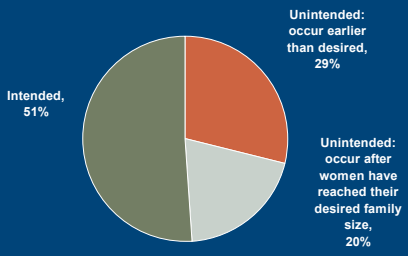


Nearly half of pregnancies in the United States are unintended



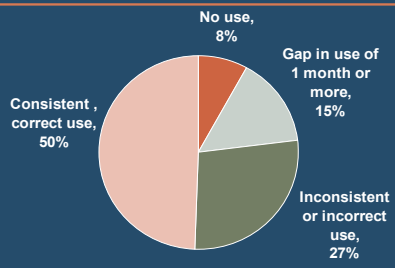
Approximately 6.4 million pregnancies per year

Most unintended pregnancies occur when women fail to use contraceptives or use their method inconsistently



3.1 million unintended pregnancies by contraceptive use during month of conception

Half of women at risk are not fully protected from unintended pregnancy



28 million adult women at risk for unintended pregnancy

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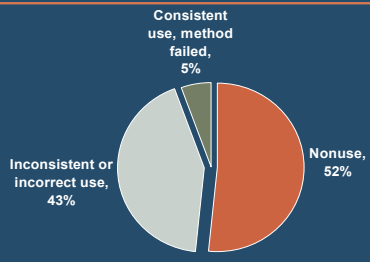
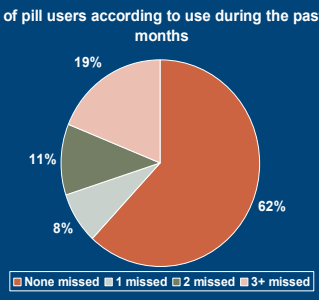
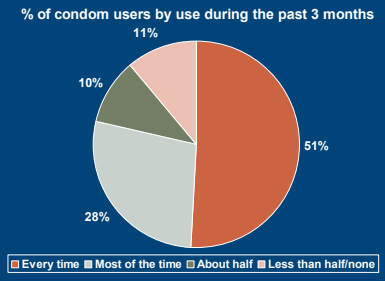


3.1 million unintended pregnancies, by women's contraceptive use during month of conception

Thirty-eight percent of women use the pill inconsistently



Sixty-one percent of couples use condoms inconsistently



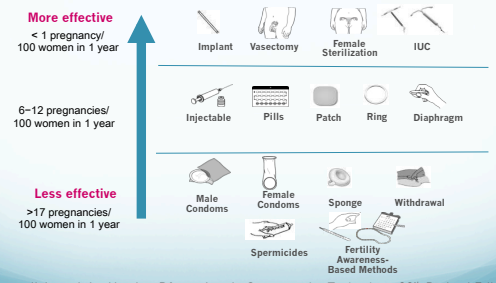
Factors with difficulty in contraceptive use

- Life changes: Relationship, residence, job/ school or personal crisis
- Socioeconomic factors
- Minority populations
- Motivation: Ambivalence about pregnancy

All methods are not equal

- User dependent (OCPs, Condoms) less effective than long acting
- Methods requiring frequent refills or provider visits subject to lack of access or availability

Comparing Typical Effectiveness of Contraceptive Methods



Trussell J, et al. In: Hatcher RA, et al., eds *Contraceptive Technology*, 20th Revised Edition. 2
Chart adapted from WHO 2007.

The Choice Project

Large 3 year prospective cohort study of over 9,000 women of reproductive age in the St. Louis area

Study Inclusion Criteria

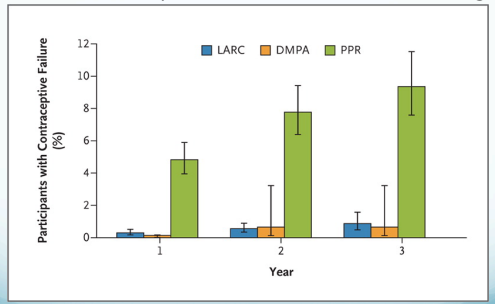
- Women 14-45 years
- Primary residency in STL City or County
- Sexually active with male partner (or soon to be)
- Does not desire pregnancy during next 12 months
- Desires reversible contraception
- Willing to try a new contraceptive method

Study Design: Prospective Cohort

Exposure		Outcome
	2–3 y	
LNG-IUS Cu-IUD Implant DMPA Pills Patch Ring Other		Unintended pregnancy Teen pregnancy Repeat abortion Abortion Continuation Satisfaction STI

ELIGIBLE

Rates of Contraceptive Failures (pregnancies) with LARC, Depo Provera, or Pills/Patch/Ring



Winner B et al. N Engl J Med 2012;366:1998-2007

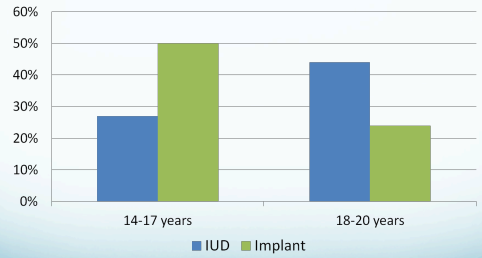
Baseline Chosen Method

	%
LNG-IUS	46.0
Copper IUD	11.9
Implant	16.9
DMPA	6.9
Pills	9.4
Ring	7.0
Patch	1.8
Other	<1.0

75%

Peipert Obstet & Gynecol 2012

Choice of LARC Methods among Adolescents



Mestad Contraception 2011

12-Month Continuation

Method	Continuation Rate (%)
LNG-IUS	87.5
Copper IUD	84.1
Implant	83.3
Any LARC	86.2
DMPA	56.2
OCPs	55.0
Ring	54.2
Patch	49.5
Non-LARC	54.7

Peipert Obstet Gynecol 2011

12-month Continuation: Adolescents Compared to Older Women

Rosenstock Obstet Gynecol 2012

CHOICE Compared to U.S.

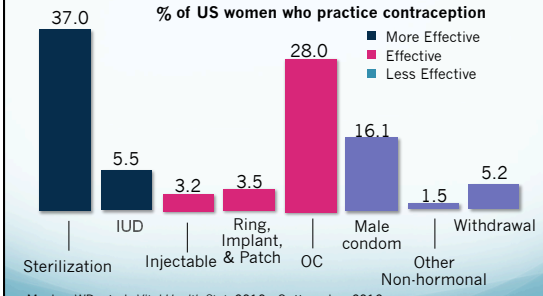
- Teen birth rate (age 15-19 years)
  - 6.3 per 1,000 teens
  - Compared to 34.3 per 1,000 nationally
- Abortion rate (women ages 15-44)
  - 6.0 per 1,000 women
  - Compared to 19.6 per 1,000 nationally
- Unintended pregnancy rate
  - 15.0 per 1,000 women
  - Cumulative: 35.0 per 1,000 women
  - Compared to 52.0 per 1,000 nationally

Peipert Obstet Gynecol 2012

Main Findings from CHOICE

- LARC methods associated with higher continuation & satisfaction than shorter-acting methods
  - Regardless of age
- LARC methods associated with lower rates of unintended pregnancy
- Increasing LARC use can decrease unintended pregnancy in the population

Contraceptive Use in the United States, 2006–2008



Mosher WD, et al. *Vital Health Stat.* 2010.; Guttmacher 2012.

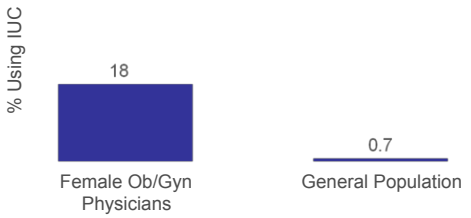
Emphasize Effectiveness in Contraceptive Choice

- "These are the most effective methods but we will support your decision for other methods"
- Permanent sterilization when appropriate-improve access to vasectomy and Essure
- Access to provider after initiating user dependent methods key in ongoing use

IUDs Underutilized in United States

- Lack of awareness
- Residual concerns dating back to Dalkon Shield
- Reluctance to have a device in uterus or anxiety about placement
- High up front costs limiting coverage/access
- Myths about IUDs
- Lawyers trolling for class action cases-negative publicity

Use of IUC by Female Ob/Gyns vs. All Women in the United States



Population Reference Bureau. 2002; The Gallup Organization. 2004.

Dispelling Myths About IUC

In fact, IUDs:

- *Are not* abortifacients
- *Do not* cause ectopic pregnancies
- *Do not* cause pelvic infection
- *Do not* decrease the likelihood of future pregnancies
- *Are not* large in size
- *Can* be used by nulliparous women

- *Can* be used by women who have had an ectopic pregnancy
- *Do not* need to be removed for PID treatment
- *Do not* have to be removed if inflammatory changes are noted on a Pap test

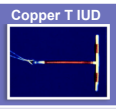
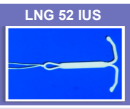
Duenas JL. *Contraception*. 1996; Forrest JD. *Obstet Gynecol Surv*. 1996; Hubacher D. *N Engl J Med*. 2001; Lippes *J. Am J Obstet Gynecol*. 1999; Otero-Flores JB. *Contraception*. 2003; Penney G. *J Fam Plann Reprod Health* Care. 2004; Stanwood NL. *Obstet Gynecol*. 2002; WHO. 2009.

IUC Available in the United States

- Copper T 380A IUD
  - Copper ions
  - Approved for 10 years of use

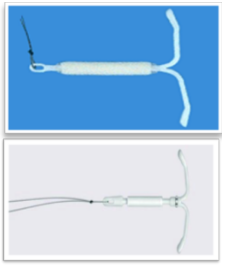
ParaGard® PI. 2013; Teva. 2013.

IUC Mechanism of Action

Mechanism of Action	Copper T IUD	LNG 52 IUS	LNG 13.5 IUS
			
Primary	• Prevents fertilization • Reduces sperm motility and viability • Inhibits development of ova	• Inhibits fertilization • Causes cervical mucus to thicken • Inhibits sperm motility and function	
Secondary	• Inhibits implantation	• Inhibits implantation	

Ortiz ME. *Contraception*. 2007; Alvarez F. *Fertil Steril*. 1988; Segal SJ. *Fertil Steril*. 1985; ACOG. 1998; Jonsson B. *Contraception*. 1991; Silverberg SG. *Int J Gynecol Pathol*. 1986.

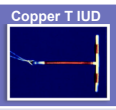
IUC Available in the United States
(continued)



- LNG 52 IUS
  - Releases 20 µg of LNG per day
  - Approved for 5 years of use
- LNG 13.5 IUS
  - Releases 14 µg of LNG per day
  - Approved for 3 years of use

Mirena® PI. 2013; Skyla™ PI. 2013.

IUC Mechanism of Action

Mechanism of Action	Copper T IUD	LNG 52 IUS	LNG 13.5 IUS
			
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Animated Insertion: LNG 52 IUS

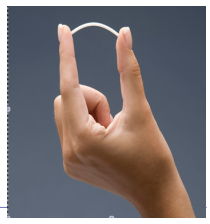
https://www.youtube.com/watch?v=zgi3mbW2YdA

Implantable Method

- Implanon/Nexplanon
  - Effective for 3 years
  - 68mg etonogestrel
  - Inhibit ovulation, suppress endometrium, thicken mucous
  - Requires specific training

Nexplanon

- Most effective reversible method
- Decreases blood loss with menstruation
- Decreases Dysmenorrhea
- Does not change BMD
- Important to counsel about the likelihood of irregular periods



Committee on Adolescent Health Care. Adolescent and long-acting reversible contraception: implants and intrauterine device. American college of obstetricians and gynecologists: 539;Oct 2012

Nexplanon

- Menstrual pattern at 3 months correlates with pattern for remaining 3 years
- Counsel upfront that bleeding pattern "worse" for most women with Nexplanon compared to Mirena
- 6-23% of users worldwide discontinued the method because of bleeding issues
- Treatment options for irregular periods
  - COC pills taken normally 1-3 months
  - Progestin-only pills taken for up to three months
  - NSAIDS especially COX-2 inhibitors 5-10d
  - Tranexamic acid 500 mg BID x 5d
  - Doxy 100mg po BID x14d

The Need for New Developments in Contraception

4.5 million women in the US

have an unmet need for contraception

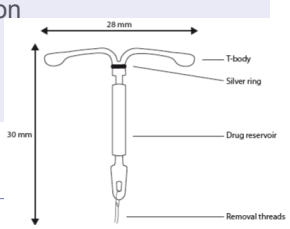
There is a need for…

NEW HIGHLY EFFECTIVE AND EASY-TO-USE METHODS	LOWER-COST METHODS	METHODS WITH FEWER SIDE EFFECTS	GREATER VARIETY OF METHODS

Finer LB, Zolna MR. *Contraception.* 2011.

FDA-Approved April 2013: LNG 13.5 IUS (Skyla™)

- Bayer HealthCare Pharmaceuticals
- LNG 13.5 mg
- Pregnancy prevention for up to 3 years
- Easy insertion and low pain reported



LNG 13.5 IUS (Skyla™) Phase 3 Study Results

	LNG 13.5
Unadjusted Pearl Index (PI)	0.33
Cumulative failure rates	0.9%
Serious adverse event (SAE)	2 cases PID
	None observed
	3 ectopic pregnancies
Cumulative risk of expulsion	4.56%

NOTE: LNG 13.5 was previously identified as LCS 12.

LNG 13.5 IUS (Skyla™) Patient Profile: Anna

- Why might LNG 13.5 IUS (Skyla™) be a good choice for Anna?
  - 22-year-old, nulliparous
  - 100 lbs./5' 2''
  - Interested in birth control method not requiring daily action
  - Interested in IUD but scared of insertion procedure

LNG 13.5 IUS (Skyla™) Patient Profile: Anna (continued)

- Why might LNG 13.5 IUS (Skyla™) be a good choice for Anna?
  - A. Low pain during placement
  - B. Lower discomfort/cramping during insertion compared with LNG 52 IUS (Mirena®)
  - C. Can last 3 years
  - D. All of these
  - E. None of these

Contraceptives Currently in Development for US

	Available 2014	*Available beyond 2014*
Hormonal	•MPA 25 mg and estradiol cypionate 5 mg **monthly injectable** •LNG/EE low-dose **transdermal patch**	•Nestorone/EE **vaginal ring** •Gestodene/EE **transdermal patch** •LNG 19.5 **IUS** •LNG 20 **IUS**
Non-hormonal		•SILCS **diaphragm** •PATH **female condom**

In Phase 3 Clinical Trial: LNG 19.5 IUS

- Bayer HealthCare Pharmaceuticals
- LNG 19.5 mg
- Similar to LNG 13.5 IUS (Skyla™)
- Well tolerated by patients
- Use for up to 5 years

Soon-To-Be-Available New Method: Monthly Injectable (Cyclofem®)

- Concept Foundation & Sun Pharmaceutical Industries
- 25 mg MPA + 5 mg estradiol cypionate
- Same formulation as injectable previously marketed in the US (Lunelle®)
- Seeking FDA approval for US

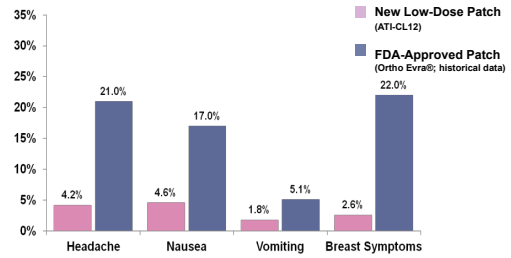
www.conceptfoundation.org/hormonal-contraception.php

Soon-To-Be-Available New Method: EE + LNG Transdermal Patch

- Agile Therapeutics
- Low-dose, once-weekly patch
- Minimizes seepage of adhesive around edge of patch ("cold flow")
- ↓ chance of residue on skin
- NDA submitted
- Decision expected 2013

Adverse Event Profile: EE + LNG Transdermal Patch

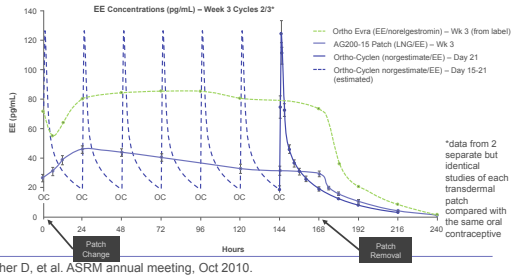
New low-dose patch showed lower levels of hormone-related side effects



Kaunitz AM, et al. May 2012.

Comparison of EE PK Profile

New EE+LNG low-dose patch has ~1/2 the EE exposure of the current norelgestromin/ethinyl estadiol patch (Ortho Evra®)



Archer D, et al. ASRM annual meeting, Oct 2010.

Future New Method: EE + Gestodene Patch

- Bayer HealthCare Pharmaceuticals
- Contains ethinyl estradiol and gestodene
- Phase 3 trial in progress
  - evaluating effectiveness, general safety, patterns of bleeding, and acceptability

EE + LNG Patch Patient Profile: Jennifer

- 23 yo
- Former patch user
- Stopped patch because exercise caused a sticky ring & breast tenderness
- She liked weekly formulation and birth control she could see and feel

EE + LNG Patch Patient Profile: Jennifer (continued)

Why might this be a good choice for Jennifer?

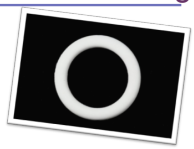
A. Half the progestin exposure of the currently available patch
B. More reliable than a combined OC pill
C. Less seepage of adhesive around the patch than with the current patch
D. Improved efficacy over the current patch

Future New Method: LNG 20 IUS

- Uteron Pharma Operations (in Belgium)
- Purpose:
  - ↓ cost
  - ↑ use from 5 to 7 years
- 20 mcg/day LNG
- Study completion ~Dec. 2018

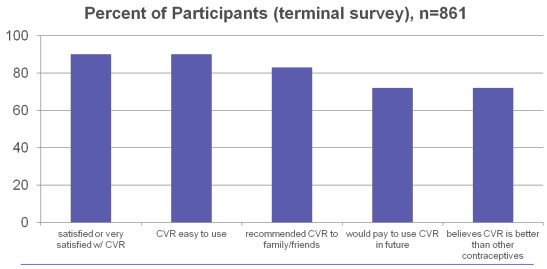
Future New Method: Nestorone/Ethinyl Estradiol 1-Yr Ring

- Population Council
- Releases150 mcg nestorone + 15 mcg ethinyl estradiol/day
- Used like existing ring (3 weeks in, 1 week out)
- Lasts 13 cycles
- Awaiting FDA approval



8.4 mm (3/8") in cross-section
58 mm (2 1/14") in diameter

Nestorone/EE 1-Year Contraceptive Vaginal Ring: Clinical Trial Results



Merkatz R. International Conference on Family Planning. Nov 2009.

Future New Method: Many Pills are in Development

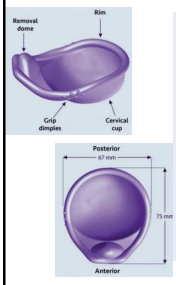
Teva
- OC continuous regimen of LNG 0.15 mg / EE 20 mcg x42d, 25 mcg x21d, 30 mcg x21d, EE mcg x 7d

Bayer
- Combined OC extended regimens w/ drospirenone 3 mg / EE 20 mcg

Merck
- OC containing nomegestrol acetate 2.5 mg, 17ß-estradiol 1.5 mg

BioSante and Pantarhei Bioscience
- OC with estrogen, progestin, and androgen

Future New Method: SILCS Diaphragm



- PATH and SILCS, Inc.
- Cervical barrier device
- One size fits most
- Developed with input from women and men in multiple countries
- Regulatory applications in Europe and US

Postpartum Contraception

- Opportunity to prevent recurrent unintended pregnancy
- Optimal time for 3rd party coverage
- No concern about luteal phase pregnancy

Postpartum contraception

- Postpartum tubal ligation
- Immediate postplacental IUDs
- Nexplanon or depo prior to discharge
- Initiate OCPs/Patch/Ring at 4 week
- Breastfeeding not concern with above
- Referral for vasectomy and Essure

Immediate postplacental IUD

- Disadvantage is higher expulsion rate than interval – about 10 % compared to 2%
- Copper or Levonorgesterol
- More women will wind up with IUD than if wait till 6 weeks postpartum for variety reasons
- New Mexioc Medicaid now paying outside of Global

Physical Examination before IUD placement

- General well being and postpartum condition
- Normal temperature
- Assessment of involution of uterus and uterine contractions
- No abnormal bleeding/evidence of infection
- Consider cleaning perineal area, particularly if stool present
- Put on a new pair of sterile gloves

Postplacental manual insertion

- Within TEN minutes of placental delivery
- The cervix is open and limp
- Allows for the passage of a hand
- Placement of the IUD high in the fundus
- Chorioamnionitis and ongoing PPH are contraindications

Technique for Postplacental IUD

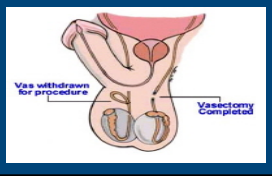
- Immediate postpartum technique with **inserter**
- Ring forceps: Grasp the anterior cervix with a ring forceps and place IUD in second ring Forceps
- Manual placement with hand

Permanent Sterilzation

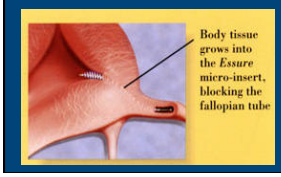
- Vasectomy
- Laparoscopic interval tubal ligation
- Essure placement of coils in tubal ostia in clinic or day surgery

Vasectomy

- Outpatient- no sclapel no needle techniques
- Lower risk than female sterilization
- Coverage by Title X unlike interval tubal ligation

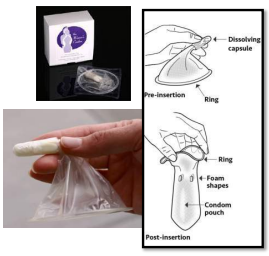


Essure



- Composition
  - Inner stainless steel core
  - Polyethylene fibers
  - Outer titinol coil
- Mechanism of action
  - Stimulates fibrous in-growth fixing implant and blocking the tube

Future New Method: PATH Women's Condom



- PATH
- Polyurethane condom pouch
- Adherence to vaginal walls improved by foam dots
- Soft outer ring
- Dissolving capsule

Emergency Contraception

- Hopes for large effect on unintended pregnancy have not been realized
- Issues of cost and accessability
- Studies demonstrate less effective in larger women (BMI or weight)
- Unprotected intercourse often a chronic not acute condition
- Still worthwhile but need to look at long acting contraceptive followup

Emergency Contraception Options Beyond Plan B prescription

- Generic Levonorgesterol available OTC without prescription since March 3 2014 labeled for 17+
- Uro
- Paragard IUD –most effective EC. Levonorgesterol IUD not studied or recommended
- Ulipristal acetate: ella©

Next Choice One Dose™ and My Way™ (generic)

- 1.5mg levonorgestrel (one pill)
- Label: Take within 72 hours after intercourse
- Recommended: up to 120 hours after sex if needed
  - Cost: $35 ($24-$42)
    - 10-20% cheaper than Plan B One-Step

ella©

- 30mg ulipristal acetate (one pill)
- Label: Take within 120 hours after intercourse
- Cost has been coming down
  online prescription + shipping now = $59
  www.ella-kwikmed.com

ParaGard® (Copper-T IUD)

- *Off label use*
- Placed within 5 days after intercourse
- Effectiveness does not decline with delay
- Placed by a trained clinician
  - Cost may be $500
- *Should be free without copay thanks to ACA for most women not working at Hobby Lobby*

Experience with IUDs for EC

Country	*Population*	*Pregnancies*	*Rate*	*95% CI*
Total	**7,034**	**10**	**0.14%**	**(0.08%- 0.25%)**
China	5629	6	0.11%	(0.05%- 0.23%)
UK	496	0	0.00%	(0.00%- 0.70%)
US	401	0	0.00%	(0.00%- 0.85%)
Italy	253	0	0.00%	(0.00%- 1.38%)
Egypt	200	4	2.00%	(0.69%- 5.03%)
Netherlands	55	0	0.00%	(0.00%- 5.93%)
Total w/o Egypt	**6,834**	**6**	**0.09%**	**(0.04%- 0.19%)**

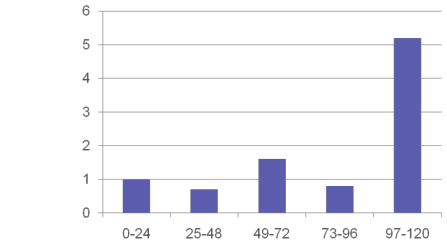
Cleland et al. 2011

Ulipristal *versus* Levonorgestrel

- Meta-analysis of two randomized studies found ulipristal superior to levonorgestrel
  - 0-24 h: OR=0.35 (95% CI, 0.11-0.93)
  - 0-72 h: OR=0.58 (95% CI, 0.33-0.99)
  - 0-120 h: OR=0.55 (95% CI, 0.32-0.93)
    - Adjusted for BMI, repeated sex, etc

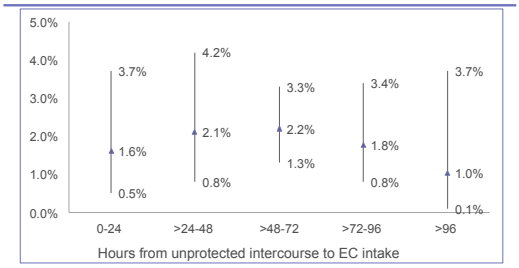
Glasier AF et al, *Lancet* 2010

Pregnancy Rates after LNg: Pooled WHO Studies



Piaggio, *Contraception* 2011

Pregnancy rates by time between unprotected sex and use of Ulipristal



Sustained efficacy over time elapsed since UPI, P=0.91

Moreau and Trussell, 2011

ECPs and Obesity

ECP failure among obese *vs.* non-obese women

- LNg: OR = 4.41, 95%CI 2.05-9.44
- Ulipristal: OR = 2.62, 95%CI 0.89-7.00

Glasier *Contraception* 2011.

The limits of efficacy of EC pills

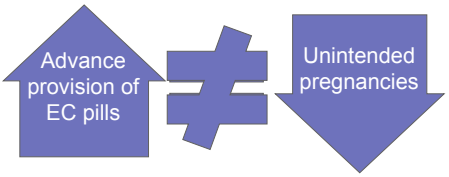
- For LNg: Weight=70 kg (154 lbs)
- For UPA: Weight=88 kg (194 lbs)

On average:

American women weigh 166 lbs

Glasier et al, Contraception 2011

Advance Provision Increases Use of ECPs…BUT



Advance provision of EC pills has not been shown to reduce rates of unintended pregnancy.

Polis, Schaffer, Blanchard *Cochrane Database Syst Rev* 2010
Raymond EG, Trussell J, Polis *Obstet Gynecol* 2007

Why No Reduction in Pregnancies?

Among women who received progestin-only ECPs in advance

45% of women who had UPI did not use ECPs they were provided

San Francisco

33% of women had UPI at least once without using ECPs they were provided

Nevada/NC

more…

Raine *JAMA* 2005, Raymond *Contraception* 2006

Use and Underuse of ECPs

Women underestimate their risk of pregnancy

- Education is needed to encourage women to use ECPs **every** time they are needed

ECPs are not used frequently enough

- Underuse of ECPs means major public health impact is unlikely

Polis, Schaffer, Blanchard *Cochrane Database Syst Rev* 2010
Raymond EG, Trussell J, Polis *Obstet Gynecol* 2007

Take-Away Points on Effectiveness

- **IUD is most effective EC option**
- *Especially with repeated unprotected intercourse*
- ***and especially if she weighs more than 195 lbs***

A drop of EC in the ocean of UPS

Summary

- Offer LARCs as most effective methods based on Choice study
- Maintain accessibility for contraception questions
- Unprotected intercourse is chronic condition- consider Paragard IUD and Ulipristal
- Postpartum LARCS now covered by Medicaid outside of global

UNM Center for Reproductive Health

- Referral site for complex contraceptive problems
- Outpatient vasectomy and Essure
- Low cost IUDs and Nexplanons through resident training grants ($125 total)
- Miscarriage management and abortion care
- (505) 925-4455
- 2301 Yale Blvd. SE, Building E, Albuquerque