

# Top Questions in Contraception

**Martin Quan, MD**

Professor of Clinical Family Medicine

Vice Chair for Academic Affairs

David Geffen School of Medicine at UCLA  
Los Angeles, CA

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## Disclosure

I have no financial interests or relationships to disclose.

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# Top Questions in Contraception

## What's New with the Birth Control Pill?

SLYND ®

NEXTSTELLIS ®

0PILL ®

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### Drospirenone POP (Slynd®)

- FDA approved May 23, 2019
- progestin-only pill (POP) aka “minipill”
- 24 days of 4 mg DSPN followed by 4 days inert
- cross between traditional POP and COC
  - contains no estrogen
  - inhibits ovulation
  - not required to take the pill at same time each day
- Pearl index: 3.2-4.0 pregnancies/100 women-yr

Kimble et al, Contraception X 2 (2020) 100020

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## Drospirenone POP Bleeding Pattern

BLEEDING PATTERN	Cycles # 2-4	Cycle # 5-7	Cycle # 11-13
Scheduled W/D bleeding	44 %	32 %	29 %
Unscheduled bleeding	57 %	50.4 %	42 %
Unscheduled spotting	61 %	51 %	42 %

Kimble et al, Contraception X 2 (2020) 100020

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## “Novel COC” (Nextstellis®)

- **Progestin type:** drospirenone 3 mg
  - analogue of spironolactone
  - progestin activity, anti- androgenic & anti-mineralocorticoid activity
- **Estrogen type:** estetrol (E4) 14.2 mg
  - natural fetal estrogenic steroid
  - inducer of liver protein synthesis
- **Pearl index:** 2.3-3.1 pregnancies/100 women-yr
- **BTB:** 15-20 percent

Expert Rev Clin Pharm 2020; 13:327-30;  
Contraception 2021;104;222-8

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## “New COC” (Con’t)

### Estetrol

- NEST- Natural Estrogen with Selective actions on Tissue
- SERM-like
- Activate beneficial estrogen receptors in vagina, endometrium, bone, and vascular system
- less effect on liver and breast

Expert Rev Clin Pharm 2020; 13:327-30  
Breast Cancer: Basic and Clinical Research Volume 13: 1-8

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## Norgestrel POP (Opill®)

- FDA approved July 13, 2023
- Ovrette® approved 1973
- first OTC oral contraceptive
- uninterrupted daily dose of 0.075 mg norgestrel
- mechanisms of action
  - inhibits ovulation
  - altered tubal motility
  - thickens cervical mucus

Contraceptive Technology 22<sup>nd</sup> edition- 2023

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## Norgestrel POP (Opill®)

- Effectiveness
  - Perfect use: 0.3/100 women-years
  - Typical use: 7/100 women-years
- Side effects
- Initiation
- Missed pill
- Cost: 3 month/\$49.99



Contraceptive Technology 21<sup>st</sup> edition- 2025

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## Top Questions in Contraception

Can a Woman on a GLP-1 Receptor Antagonist Effectively Use an OCP?



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## COC and GLP-1 RA Interaction

- concerns raised re ? interaction with COCs
- Kapitza et al<sup>1</sup>: no change in AUC<sub>1-24h</sub> with semaglutide (at doses up to 1 mg weekly) for EE 30ug/LNG 0.15<sup>1</sup>
- Skelley et al<sup>2</sup>: significant change in AUC with tirzepatide in patients on EE 30ug/NGM 0.25
- recommendation: for tirzepatide, switch to non-oral method or use B/U x 4 wks following initiation or dose



1. J Clin Pharm 2015;55(5):497  
2. J Am Pharm Assoc 2024;64:204

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## Top Questions in Contraception

How Do You Choose Among the  
Different IUDs Available ?



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# IUD: Making a Comeback

- **highly effective**
  - copper IUD: 0.8 pregnancies /100 women-yr
  - LNG-IUD: 0.4 pregnancies/100 women-yr
- **convenient**
- **high user satisfaction rate**
- **no increased risk of PID<sup>1-3</sup>**

2023: 22<sup>nd</sup> edition Contraceptive Technology

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## Available IUDs

PARAGARD



MIRENA



SKYLA



LILETTA



KYLEENA



MIUDELLA



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## Miudella

- FDA approved 2/24/25 (Sebala Pharm)
- 175 mm<sup>2</sup> of copper
- 30 x 32 mm nitriol frame, pre-cut string
- preloaded in inserter barrel 3.7 mm
- approved for 3 years, available only through the Miudella REMS Program
- phase 3 study is ongoing to evaluate efficacy, safety, and tolerability up to 8 years



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## Miudella: 3-year Phase III Trial

- 1620 subjects, successful placement 98.8%
- efficacy: 1-yr Pearl Index 0.94, pregnancy rates at 1 yr and cumulative 3 yr of 1.26% and 2.47%, respectively
- rates of discontinuation due to pain and/or bleeding less than reported for TCu380A for one year (8.6 % vs 11.9%) and for year three (3.7% vs 7.0%)
- device expulsions occurred in 36 (2.2%) and 63 (3.9%) participants over 1 and 3 years, respectively

Creinin MD, *Contraception*. 2025;143:110771.

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## IUD Selection

IUD type	# years approved	Diameter (mm) Insertion barrel	Frame size (mm)	Dose of LNG (mg)	LNG release at 60 days	Amenorrhea at year 1 (year 3)
Paragard	10	4.4	36 x 32	0	0	N/A
Miudela	3**	3.7	30 x 32	0	0	N/A
Mirena	8	4.75	32 x 32	52	20 mcg/d	20 % (36%)
Liletta	8	4.75	32 x 32	52	20 mcg/d	20 % (36%)
Kyleena	5	3.8	30 x 28	19.5	15.3 mcg/d	12 % (20%)
Skyla	3	3.8	30 x 28	13.5	10 mcg/d	6% (12%)

Contraception. 2019 Aug;100(2):128-131.

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## Top Questions in Contraception

How Do You Manage Breakthrough  
Bleeding Associated with the  
Progestin Subdermal Implant?

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## Etonogestrel Implant Adverse Reactions

- irregular vaginal bleeding: 50-60 %
  - 23 % discontinue early due to bleeding concerns <sup>1</sup>
- amenorrhea: 30-40 %
- acne: 15 %
- mastalgia: 9.1 %
- headache: 8.5 %
- weight gain: 6.4 %

J Fam Plann Reprod Health Care 2014;40:158-160  
Ob Gyn Clin North Am 2015;42:593-602

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## Management of BTB with Implant

- NSAIDs: Ibuprofen\* 600 mg TID x 5 days or Naproxen\* 500 mg BID x 5-7 days
- COC\*: 0.30 mg EE + 0.15 L-NG x 10-20 d
- Estrogen\* :
  - CEE 1.25 mg/d x 7-14 days
  - Ethinyl estradiol 20 mcg/d x 10-20 days
  - Micronized estradiol 2 mg/d x 7-14 days
  - Transdermal patch 0.1 mg x 7-14 days

\* OFF-LABEL USE

2024 CDC MMWR 2024;73(3):18-23  
Ob Gyn Clin North Am 2015;42:593-602  
Ob Gyn 2015;126:508-13

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## Management of BTB with Implant

- Mefenamic acid (Ponstel ®)\*: 500 mg BID-TID x 5-7 days
- Doxycycline\* 100 mg BID x 5-7 days
- Tranexamic acid (Lysteda®)\*- antifibrinolytic agent 500 mg BID x 5-7days
- Tamoxifen\* 10 mg BID x 7days
- Norethindrone acetate 5-10 mg daily x 7 days

\* OFF-LABEL USE

J Fam Plann Reprod Health Care 2014;40:158-160  
Ob Gyn Clin North Am 2015;42:593-60  
Obstet Gyn 2018;132(4):888

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## Top Questions in Contraception

In a Woman on a COC, How Do You Advise Them Regarding “Missed Pills”?

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## OCP Problem: Missed Pills

### Basic principles:

- 7 days of continuous use of COC is required to ensure ovulation is suppressed
- some may demonstrate some follicular activity prior to end of a 7 day pill-free period
- degree of suppression varies with dose of COC

1. MMWR 2013;62:No. RR 26-27  
2. Webberly, Current Obstet Gynecol 2006;16:21

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### **“Reduced HFI” OCPs** **Reduced Number of Inert Pills**

#### • **Mircette**

21 d (20 mcg EE + 0.15 DSG) + 4 d 20 mcg EE + 3 days inert

#### • **Loestrin 24 Fe**

24 d (20 mcg EE + 1 mg NA) + 4 d 75 mg Fe

#### • **“Yaz”**

➤ 24 d (20 mcg EE + 3 mg DRSP) + 4 d inert

#### **“Lo Loestrin”**

24 d (10 mcg EE + 1 mg NA) + 2 d 10 mcg EE + 2 d inert

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## OCP Problem: Missed Pills

Week # 1: **HIGH RISK (even if one pill missed)**

- back-up method x 7 days
- consider EC

Weeks 2-3: **CONCERN IF MISS 2-3 pills**

- back-up x 7 days
- consider EC

**\*\* if week # 3: skip inert pill week and begin new pill packet**

1. MMWR 2013;62:No. RR 26-27  
2. Webberly, Current Obstet Gynecol  
2006;16:21

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## Top Questions in Contraception

Does the Birth Control Pill Cause  
Cancer?

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## OCPs and Cancer

### RCGP Study

- inception cohort study of 23,377 everuser, 23,796 never-users.
- 388,505 women-yrs for non-users, 884,895 women-yrs for ever-users

#### Cancer

#### RR

Ovary	0.67 (0.60-0.89)
Uterine	0.66 (0.48-0.89)
Cervix	1.31 (0.84-2.04)
Breast	1.04 (0.91-1.17)

Am J Ob GYN 2017;216:580.e1-9)

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## Hormonal Contraceptives and Breast Ca

### Danish Sex Hormone Registry Study

prospective cohort study: 1.8 million women, mean F/U 10.9 yrs: 11,517 cases of breast cancer

Contraceptive method	Relative Risk (95% CI)
Current or recent use of hormonal contraceptive	1.20 (1.14-1.26)
Combined OCP	1.19 (1.13-1.26)
LNG- IUD	1.21 (1.11-1.33)

N Engl J Med 2017;377:2228-39

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## Hormonal Contraceptives and Breast Ca

### Danish Sex Hormone Registry Study

#### Criticisms:

- RR= 1.20 is small and of ? significance
- LNG-IUD risk not related to duration, no risk with progestin implant and POPs
- confounding factors: breastfeeding, alcohol use, physical activity



N Engl J Med 2017;377:2228-39

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## Hormonal Contraceptives and Breast Ca

**ABSOLUTE RISK:** 13 additional cases of breast cancer per 100,000 person-years.

**15 yrs to 49 yrs age group:**

one extra case of breast cancer per 7,690 women per year.

**women < 35 years:**

one extra case of breast cancer per 50,000 women per year



N Engl J Med 2017;377:2228-39

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## Risk Factors for Breast Cancer

	<u>RR</u>
Breastfeeding	0.86
First pregnancy after 30 yrs	1.48
Obesity (BMI > 30)	1.18
BMI > 30 after menopause	1.48
Alcohol (2 drinks/day)	1.21
Alcohol (> 3 drinks)	1.38
High saturated fat intake	1.3-2.0
Eating 1/4 grapefruit/day	1.20

Clin Obstet Gynecol 2001;54:96-102  
Climacteric 2008;11:108  
Clin Adv Hematol Oncol 2016;14:790-7  
Am J Prev Med 2017;53(3 supp 1):S40-6

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## Top Questions in Contraception

What's New with Non-hormonal  
Contraceptive Methods?

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## Novel Contraceptive Options

### Non-Hormonal

- **Birth control app:**  
**Natural Cycles ®**  
**FDA approved August 2018**
- **Vaginal pH modulator**  
**Phexxi ®**  
**FDA approved August 2020**



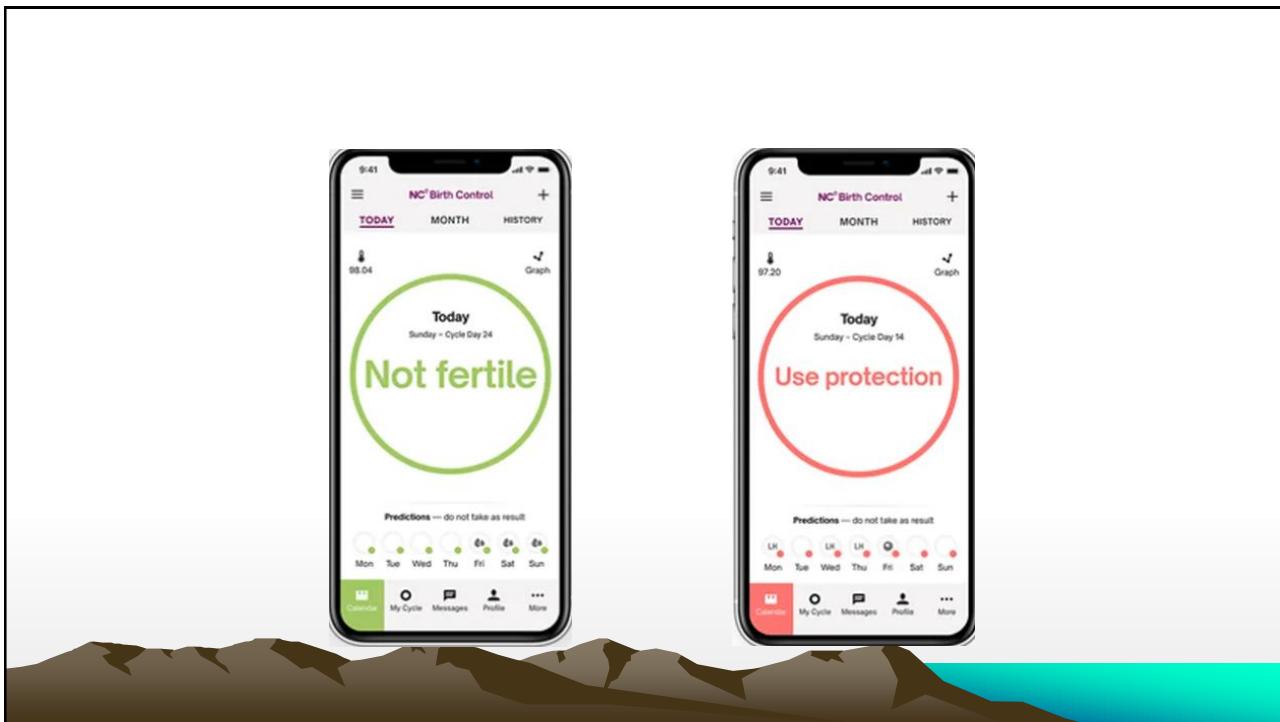
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## Birth Control App

- **first digital contraceptive method**
- **app makes use of an algorithm which determines daily fertility status based on BBT and menstrual data**
- **Pearl Index: 6.9 pregnancies/100 women-yrs**
- **Cost: \$9.99 per month, \$89.99 for one year**
- **FDA okays pairing of app with a wearable device that monitors temperature (2021)**



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Contraception 2017;96:420

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## Wearables



OURA RING



Apple® Watch SERIES 8 +

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## Vaginal pH Modulator

- **prescription vaginal gel: lactic acid (1.8%), citric acid (1%), potassium bitartrate (0.4%)**
- **MOA: sperm become immobilized at pH 3.5-4.5**
- **on-demand: one applicatorful (5 g) up to one hour before each act of vaginal intercourse**
- **can be used with condoms, diaphragm, cap, BCPs**

Contraception 2017;96:420

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## Vaginal pH Modulator

- **Efficacy: typical use- 14 pregnancies/100 women-yr**
- **Adverse effects: vaginal burning (18%), itching (14%), vaginal candidiasis (9.1%), UTI (9%)**
- **Male partner: 9.8% local discomfort (e.g. burning, itching, etc.)**
- **cost: box of 12 applicators: \$250**



Contraception 2017;96:420

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## Top Questions in Contraception

What Is the Status of Emergency Contraception?



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# Emergency Contraception (EC)

- Underutilized means for reducing the number of unintended pregnancies
- Prior to September 1998, no FDA-approved product for use as an emergency contraceptive
- 2 dedicated EC methods

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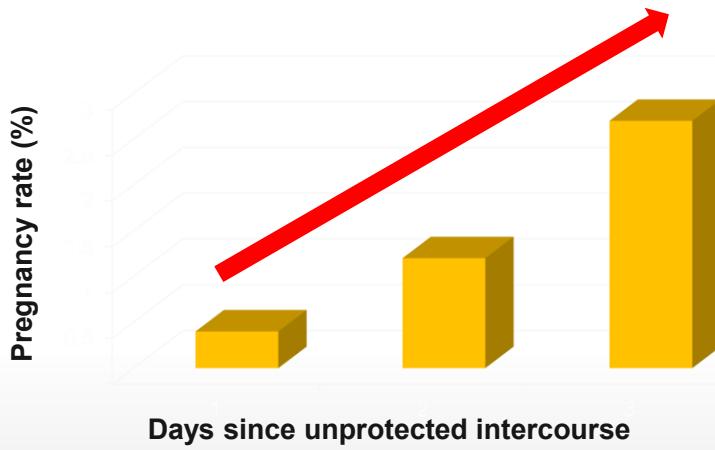
## LNG-based EC

- Progestin-only method, FDA approval of 2-step option in 1999
- One-step option (1.5 mg LNG as single dose within 72 hours of unprotected coitus) approved 7/09 (Plan B One Step®, Next Choice®, My Way®, etc.)
- OTC in 2006 for women 18+ yrs
- FDA approval of OTC use for all in 2013

\* LNG = Levonorgestrel

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## Pregnancy Rate vs Day of Administration of LNG- EC



Lancet 2008;352:428-433

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## Ulipristal Acetate (ella®)

- Progesterone receptor modulator
- FDA approval in August 2010
- One tablet (30 mg) as a single dose
- Blocks ovulation by suppressing LH surge even after it begins
- Effective up to 120 hours after unprotected intercourse and superior to Plan B

Women Health 2020;60(3):241-8 .

Chao Y, et al. Canadian Agency for Drugs and Technologies in Health; 2018 Nov 29. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK538737/>

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# Top Questions in Contraception

## Is There a Weight Limit on the Use of Emergency Contraception?

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### LNG-EC Efficacy and Weight

Contraception 2011; 84(4):363-367

WHO study of 3,893 women

#### Weight

BMI < 25

BMI 25-30

**BMI > 30**

#### R.R. of pregnancy

1.0

2.09 (CI, 0.86–4.87)

**4.41 (CI 2.05–9.44 )**

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## Pregnancy Rate After LNG-EC, By Weight

Weight, in kilograms

	<55 kg	55-65 kg	65-75 kg	75-85 kg	> 85 kg
N total	349	608	426	155	193
N pregnancies	3	8	6	10	11
% pregnancies	0.9	1.3	1.4	6.4	5.7
95% CI	0.2-2.5	0.6-2.6	0.5-3.0	3.1-4.5	2.5-6.0

Kapp et al, Contraception 2015;91:97-104

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## Ulipristal and BMI

Contraception 2011; 84(4):363-367

WHO study of 3,893 women

### Weight

BMI < 25

BMI 25-30

BMI > 30

- although less effective in obese women, ulipristal retains efficacy in women with BMI <35

### R.R. of pregnancy

1.0

0.97 (CI, 0.27–2.83)

2.62 (CI, 0.89–7.00)

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## LNG-EC + Piroxicam

Li et al, Lancet 2023; 402: 851–58

- RCT trial in Hong Kong of 886 women requiring LNG-EC randomized to piroxicam 40 mg versus placebo
- primary outcome: percentage of pregnancies prevented out of those predicted on a standard model
- pregnancy rate: 0.2% in piroxicam group vs 1.7% in placebo (OR= 0.2, p=0.036)
- piroxicam prevented 97% of expected pregnancies vs 63% in the LNG-EC + placebo



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## Emergency Contraception: Off-Label IUD Use

- Non-hormonal IUDs used for 40+ years as EC
- Insert within 5 days of unprotected coitus
- Pregnancy rate: 0.09% (less than one in a thousand)
- Patients half as likely to be pregnant one year after use of IUD vs LNG as EC

Obstet Gynecol 2015;126(3):e1-e11  
Turok et al, Contraception 2014;89:222-8

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## Top Questions in Contraception

Can the LNG-IUD Be Used Instead of the Copper IUD for Emergency Contraception?

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### Emergency Contraception: Off-Label IUD Use

- Randomized non-inferiority trial comparing LNG-IUD (355 women) vs Cu<sup>+</sup> IUD (356 women)
- Insert within 5 days of unprotected coitus
- Pregnancy rate: 0.3% in LNG-IUD and 0% in Cu<sup>+</sup> IUD
- Absolute difference 0.3% consistent with non-inferiority (95% CI, -0.9 to 1.8)
- LNG-IUD comparable to copper IUD as EC

Turok et al, N Engl J Med 2021;384:335-44.

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# Top Questions in Contraception

## Summary

- two novel OCPs are available which offer potential advantages
- LARCS are highly effective and safe devices with side effects can be effectively managed
- novel non-hormonal methods are available which show promise
- EC is a powerful but still underutilized option for reducing the number of unintended pregnancies



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A nulliparous female is seen by you and for counseling with a history of dysmenorrhea. She indicates she would like to avoid development of amenorrhea which she experienced in the past while on a low-dose oral contraceptive.

### Which One of the IUDs Would Be Preferred?

- Paraguard
- Miudella
- Mirena
- Kyleena
- Skyla

## Which One of the Following Is True Regarding the FDA-approved Digital Contraception App?

- A. Its efficacy is comparable to the intrauterine device
- B. Its efficacy is comparable to contraceptive sponge
- C. It is available only with prescription
- D. It can be paired with an Apple watch

