

Top Questions in Contraception

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Disclosure

I have no financial interests or relationships to disclose.

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?

- A. Paraguard
- B. Miudella
- C. Mirena
- D. Kyleena
- E. 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

Top Questions in Contraception

What's New with the Birth Control Pill?

SLYND ®

NEXTSTELLIS ®

OPILL ®

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®)

FDA Approval April 2021

- **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)

FDA Approval April 2021

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 22nd 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 21st 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 al¹: no change in AUC_{1-24h} with semaglutide (at doses up to 1 mg weekly) for EE 30ug/LNG 0.15¹
- Skelley et al²: 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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Available IUDs

PARAGARD



MIRENA



SKYLA



LILETTA



KYLEENA



MIUDELLA



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Miudella

- FDA approved 2/24/25 (Sebala Pharm)
- 175 mm² 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%)

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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 ¹
- 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

Danish Sex Hormone Registry Study

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 ¼ 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 suppl 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

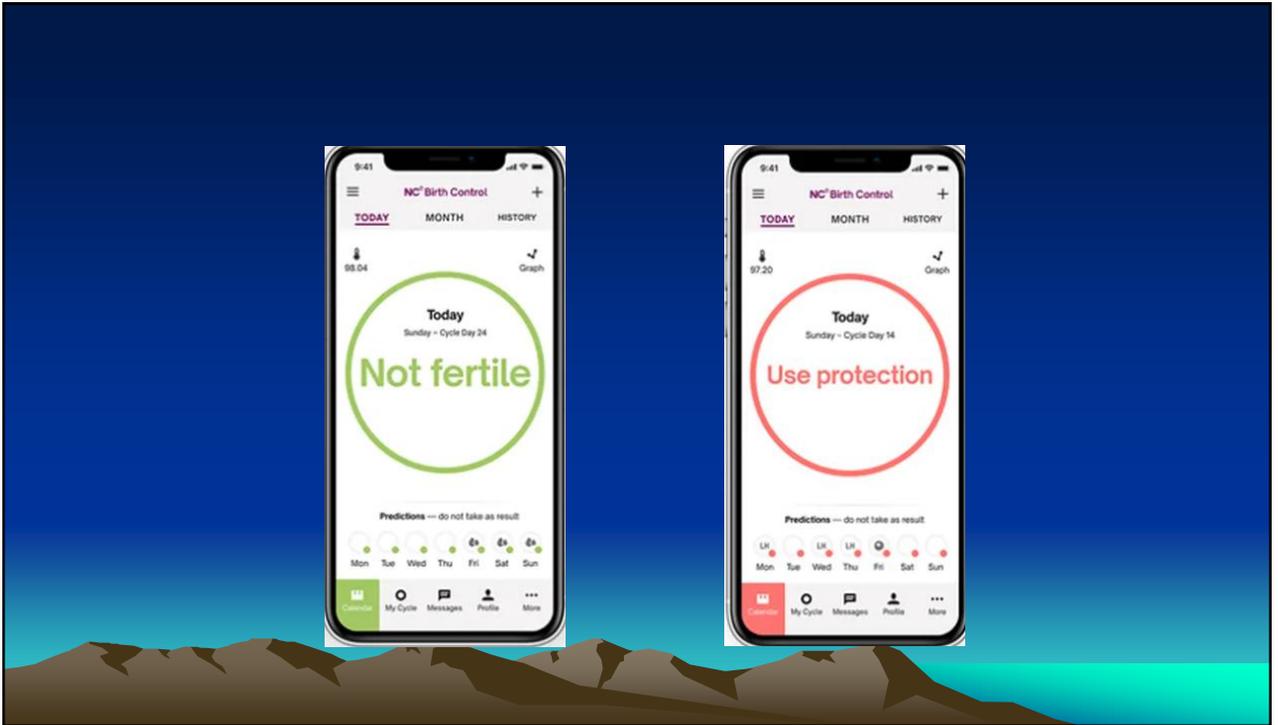
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Birth Control App

- 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)

Contraception 2017;96:420

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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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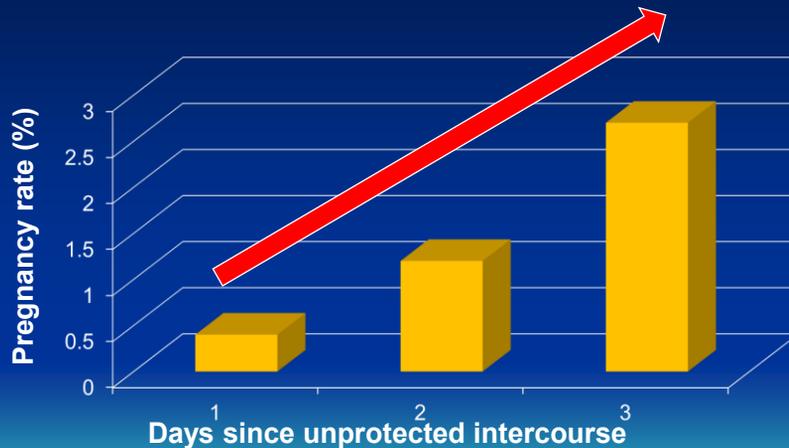
LNG-based EC

- 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

R.R. of pregnancy

1.0

0.97 (CI, 0.27–2.83)

2.62 (CI, 0.89–7.00)

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

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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⁺ IUD (356 women)
- Insert within 5 days of unprotected coitus
- Pregnancy rate: 0.3% in LNG-IUD and 0% in Cu⁺ 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