EMERGENCY CONTRACEPTION

Courtney Forbis, MD, MS
Assistant Professor
UNM Department of Obstetrics and Gynecology

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Learning Objectives

- Discuss the ways the use of emergency contraception (EC) is affected by restrictions, myths, and under-use
- Discuss indications and medical contraindications for EC
- Understand the mechanism of action and effectiveness for available forms of EC
- Discuss current data that support the use of hormonal intrauterine devices (IUDs) for EC

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Outline

- What is EC? Why do we need it?
- Legal history and barriers to access
- Population impact
- Types of EC used in the United States
- Mechanism of action and effectiveness
- Safety
- Screening and provision
- Side effects
- Effects of obesity and medication interactions
- Patient cases

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What is emergency contraception?

- WHO definition
  - *"Emergency contraception refers to methods of contraception that can be used to prevent pregnancy after sexual intercourse. These are recommended for use within 5 days but are more effective the sooner they are used after the act of intercourse."*
- Methods available
  - *Ulipristal acetate (UPA)*
  - *Levonorgestrel (LNG)*
  - *IUDs*
    - Copper and LNG

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Why do we need emergency contraception?

- Approximately 50% of pregnancies in the United States are unintended (mistimed or unwanted)
- Around 10 million couples have sexual intercourse every night in the United States
- Approximately 27,000 condoms break or slip each year in the United States
- Even perfect contraceptive use can result in failure and pregnancy
  - *COCs, patch, and ring have a failure rate of ~7% per year (Guttmacher institute)*
  - *Injectable contraception has failure rate of ~4% per year*
  - *IUDs and implants have a less than 1% failure rate per year*

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Indications for EC

- No use of contraception at time of coitus
- Male condom slippage or breakage
- Female condom incorrectly placed, dislodged, or torn
- Missing 3+ consecutive combined oral contraceptive pills
- 3 or more hours late taking progestin-only contraceptive pill
- More than 14 days late getting Depo-Provera injection
- 2 or more days late starting new vaginal ring or patch
- Failed attempt at coitus interruptus

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Legal history

- In 1999 FDA approved the first two dose regimen of 750mcg levonorgestrel (LNG) pills for EC
  - *In 2009 single pill version was introduced and generic made available*
- In 2006 FDA approved over the counter (OTC) access to women age 18 or older
- In 2009 a US judge ordered the FDA to allow women age 17 to acquire LNG EC without prescription
- In June 2013, Obama administration reversed age restriction

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Restricting access

- **Texas** excludes EC as one of the services included in the state's family planning program
- **Arkansas and North Carolina** exclude EC from contraceptive coverage mandate
- Seven states (**Arizona, Arkansas, Connecticut, Georgia, Idaho, Mississippi, and South Dakota**) explicitly allow pharmacists to refuse to dispense contraceptives, including emergency contraception
- Three states (**Arizona, Louisiana, and Mississippi**) allow pharmacies to refuse to dispense emergency contraception

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Barriers to access

- Sometimes oral EC is not stocked in pharmacies
  - *Studies estimate only an average of 3-10% of pharmacies report the product is in stock*
- Not having EC displayed as OTC medication and keeping EC in theft-proof boxes that must be unlocked by pharmacy staff result in physical barriers
  - *Patients may not want to ask staff for assistance*
  - *Can produce a sense of shame and interfere with confidentiality*
- High costs
- Lack of awareness among patients/providers
- Lack of advanced provision of oral EC

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Myths and false science

- Language on label of EC can provide misleading information and thus result in false science used by those opposed
  - *(may also prevent) "attachment of a fertilized egg to the uterus (implantation)" implies that EC causes abortion*
- Common myths stated among patients include
  - *EC will cause an abortion or harm a pregnancy*
  - *EC will prevent future fertility*
  - *EC is dangerous*
  - *It is unsafe to take multiple doses of EC*

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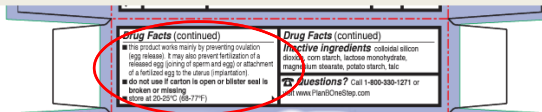

Drug Facts (continued)
- this product works mainly by preventing ovulation (egg release). It may also prevent fertilization of a released egg (joining of sperm and egg) or attachment of a fertilized egg to the uterus (implantation).
- **do not use if carton is open or blister seal is broken or missing**
- store at 20-25°C (68-77°F)

Drug Facts (continued)

Inactive ingredients colloidal silicon dioxide, corn starch, lactose monohydrate, magnesium stearate, potato starch, talc

Questions? Call 1-800-330-1271 or visit www.PlanBOneStep.com

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Who is using EC?

- Statistics from National Survey of Family Growth showed that among women age 22-49, 24% had ever used emergency contraception (2017-2019 data)
  - *Of these users, incidence was increased among those with higher level of education*
- EC (both IUDs and pills) is largely underused in the United States

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Emergency department provision

- Estimated that as many as 22,000 pregnancies resulting from sexual assault each year could be prevented by EC[1]
- 20 states and the District of Columbia require emergency rooms to provide information about emergency contraception to sexual assault victims. (Guttmacher)
- 16 states and the District of Columbia require emergency rooms to dispense the drug on request to sexual assault victims. (Guttmacher)
- Likely a missed opportunity

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Population impact

- Systematic review by Raymond et al[2] showed that increased access to EC *enhances use* but does not reduce unintended pregnancy rates
- RCT by Raymond et al[3] involving 1,490 participants *showed increased use of method with advanced access* (two packs dispensed in advance) with no increased rate of STIs but no reduction in pregnancy rates
- *No studies have shown evidence of increased sexual risk taking or increased rates of STIs*
- In a RCT of Egyptian women where LNG EC was used as supplement to lactational amenorrhea, pregnancy rates were lower in the group that received EC provision (0.8% vs 7.3%)

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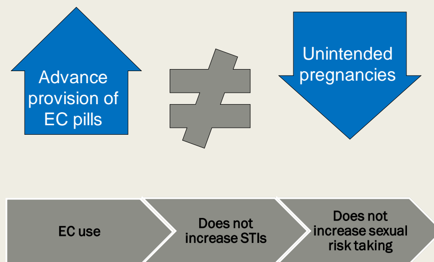

EC use → Does not increase STIs → Does not increase sexual risk taking

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Current options for EC

- Copper IUD
- UPA
- LNG
- LNG IUD

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Copper IUD

- Highest efficacy of all EC
- Not FDA labeled for EC
- Pregnancy rate of less than 0.1%[5]
- Can be inserted up to 5 days following coitus
- No effect on ovulation, primary effect is to prevent fertilization
- Inhibits sperm function, fertilized egg transport, and implantation
- Common side effects
  - *Bleeding and cramping*

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Copper IUD

- Advantages
  - *Can be left in place for highly effective long acting reversible contraception (12 years)*
  - *Highly effective form of EC and general contraception*
- Disadvantages
  - *Cost (up to $1000 if no insurance)*
  - *Timing may be tricky*
  - *Must be inserted by trained health care provider*

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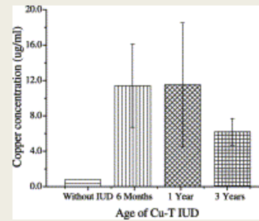
Effect of copper on sperm function

- Most studies were performed in the 1970s and 1980s
- Copper ions thought to inhibit sperm motility
  - *Reduces oxidative processes and glucose consumption, both reduce mobility*
- Higher Copper ion concentration results in higher inhibition of sperm



Arancibia V, Peña C, Allen HE, Lagos G. Characterization of copper in uterine fluids of patients who use the copper T-380A intrauterine device. Clin Chim Acta. 2003 Jun;332(1-2):69-78. doi: 10.1016/s0009-8981(03)00124-4. PMID: 12763282.

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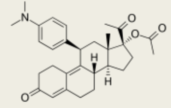
Ulipristal acetate (UPA)



- Approved by FDA in 2010
- Selective progesterone receptor modulator (SPRM)
- Inhibits or delays ovulation even after LH has started to rise
  - *Suppresses follicular growth*
- May alter endometrium

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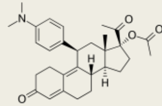
UPA



- Single 30mg dose taken up to 120 hours following coitus
- Rapidly absorbed; peak plasma concentration 0.5-3 hours after ingestion
- Most effective oral EC
- Higher efficacy than levonorgestrel (between 62-85% effective)[6]
- Only available by Rx
- Online prescription available (www.ella-kwikmed.com)
- 2016 US selected practice recommendations are to delay resumption of hormonal contraception for up to 5 days after the use of UPA

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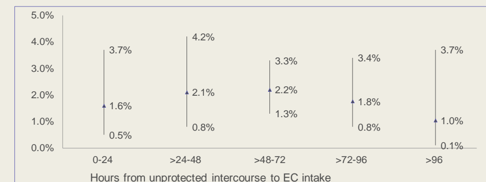
Efficacy of UPA



Efficacy is sustained over time

Moreau C, Trussell J. Results from pooled phase III studies of ulipristal acetate for emergency contraception. *Contraception.* 2011;84(3):308.

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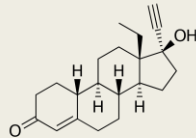
Levonorgestrel



- Single dose of 1.5mg dose approved in 2009
- Inhibits ovulation but ineffective after LH surge
  - *Not effective at preventing ovulation when follicle reaches 15-17mm*[7]
- Most effective if taken as soon as possible
- Postponing by 12 hours increases pregnancy by 50%
- No effect on implantation
- OTC cost $40-60 (may be cheaper with Rx)
- Many clinics, including Planned Parenthood, have LNG EC available at a sliding scale cost for those without insurance or low income

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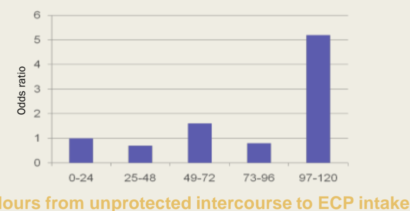
Efficacy of LNG



Hours from unprotected intercourse to ECP intake

Piaggio G, Kapp N, von Hertzen H. Effect on pregnancy rates of the delay in the administration of levonorgestrel for emergency contraception: a combined analysis of four WHO trials. *Contraception.* 2011;84:35-9.

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LNG IUD as EC

- A randomized, noninferiority trial of 638 patients investigated the efficacy of LNG 52 mg compared to the copper IUD within 5 days of unprotected intercourse[11]
- The trial demonstrated a 0.5% (95% CI 0.01% to 1.7%) failure rate for the LNG 52 mg IUD as compared to a 0% (95% CI 0%–1.1%) failure rate for the copper IUD.
- *The LNG 52 mg IUD was found to be noninferior to the cop- per IUD for EC*
- SFP recommends LNG 52mg IUD be used as first line method for EC

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LNG IUD as EC

- When given the choice, women prefer the LNG IUD to the copper IUD as EC
  - *In a study by Sanders et al in 2017, of 188 women enrolled, 38% chose copper, 63% chose LNG*
  - *Higher satisfaction rates with LNG IUD at 12 months*

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IUDs as EC

Table 2

Continuation and satisfaction at 12 months by emergency contraception choice

EC chosen	Enrolled (n)	Followed up at 12 months (n)	Continuing use, n (%)	Very satisfied or satisfied, n (%)[a]	Neutral, n (%)[a]	Very unsatisfied or unsatisfied, n (%)[a]
LNG IUD+	110	94	66 (70)	41 (71)	12 (21)	5 (8)
Copper IUD	66	53	32 (60)	17 (65)	5 (19)	4 (15)

Key: IUD, intrauterine device; LNG IUD+: same-day 52 mg levonorgestrel IUD plus 1.5 mg oral levonorgestrel; CU IUD: copper IUD.

[a]Women continuing device use completed satisfaction questioning [completion of satisfaction question 84/98 (86%)].

Sanders JN, Turok DK, Royer PA, Thompson IS, Gawron LM, Storck KE. One-year continuation of copper or levonorgestrel intrauterine devices initiated at the time of emergency contraception. Contraception. 2017 Aug;96(2):99-105. doi: 10.1016/j.contraception.2017.05.012. Epub 2017 Jun 5. PMID: 28596121; PMCID: PMC6040824.

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Combined oral contraceptives as EC

- Referred to as the Ypzpe method
- Less efficacy, more side effects
  - *Up to 50% experience nausea, 20% experience vomiting*
- **Not currently recommended given more effective options**
- Four case reports of stroke following Yuzpe method

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Old methods for EC

- Preven
  - *Approved in 1998, discontinued 2004*
  - *Essentially a Yuzpe regimen available as prescription*
  - *4 pills containing 0.25mg levonorgestrel and 0.05mg EE*
- High dose ethinyl estradiol
  - *5-10mg given daily x5 days*
  - *High incidence GI side effects*
- Danazol
  - *Low efficacy*
- Diethylstilbestrol (DES)
  - *25-50mg*

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Other potential options for EC

- Mifepristone:
  - *Available in China, Vietnam, & Russia*
  - *Anti-progesterone effects prevent ovulation and disrupt luteal-phase events*
  - *Dose: 10mg within 120 hours of unprotected intercourse*
  - *Equal efficacy to 150mg Levonorgestrel (meta-analysis in China showed lower failure rate for mifepristone)*
- Meloxicam
  - *COX-2 Inhibitor*
  - *Dose: 30mg per day x5 days*
  - *Compared effectiveness not studied*

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Mechanism of action of EC

Method	MoA
Copper IUD	Prevention of fertilization, affects sperm viability and function
Ulipristal acetate	Delayed ovulation, inhibits follicular rupture even after LH has started to rise
LNG (oral)	Impair ovulation and luteal function, delays follicular development if administered before LH rise
LNG (IUD)	May interfere with sperm transport, sperm capacitation, and oviduct transport

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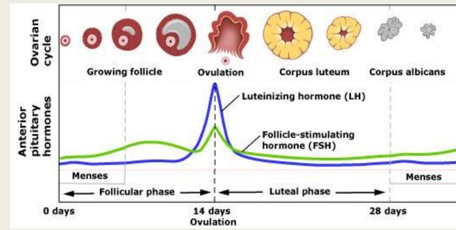

Ella

PlanB

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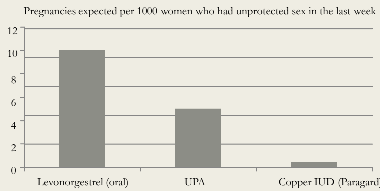
EFFECTIVENESS BY METHOD



Raymond E, et al. 2004; Task Force on Postovulatory Methods of Fertility Regulation. 1998; Trussell J, Raymond EG 2011; Fine P, et al. 2010; Glasier AF, et al. 2010.

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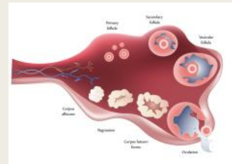
UPA vs. LNG effectiveness

- In comparative trials, UPA is more effective than LNG
  - *Odds of pregnancy were 64% lower in UPA users when taken during first 24 hours*
  - *Odds of pregnancy were 42% lower in UPA users when taken up to 72 hours*[6]



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Medical eligibility criteria

Condition	Copper IUD	UPA	LNG	COC
Pregnancy	4	N/A	N/A	N/A
Breastfeeding	1	1	1	1
H/O ectopic	1	1	1	1
H/O bariatric sx	1	1	1	1
CV disease	1	2	2	2
Rheumatoid arthritis	1 (2 if on immuno-suppression)	1	1	1
Migraine	1	1	1	2
IBD	1	1	1	1
Liver dx	1	2	2	2
Solid organ transplant	3 if complicated, 2 if uncomplicated	1	1	1
Repeated EC use	1	1	1	1
Sexual assault	2	1	1	1
Obesity (BMI>30)	1	2	2	2
CYP3A4 inducers	1	2	2	2

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Safety of EC

- There are no contraindications to EC except known pregnancy
  - *No known risk of birth defects if given and pregnancy is undetected*
- No increased risk of ectopic pregnancy

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Repeated use

- Repeated use likely safe
- Multiple studies have showed that LNG administered multiple times per cycle causes no serious adverse events
- Repeated use of UPA at 30mg dose not specifically studied, but studies have shown safety at 5mg and 10mg dose for treatment of fibroids
- Chance of pregnancy following repeated use of progestin-only EC is 20%[4]

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Pregnancy rates with repeated unprotected intercourse

Repeated UPI	Ulipristal	LNG
No	1.0%	1.9%
Yes	5.6%	7.3%

Glasier A, Cameron ST, Blithe D, et al. Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel. *Contraception*. 2011;84:363-7.

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Breastfeeding

- Not considered a contraindication to oral EC use
- Breastfeeding should not be interrupted following LNG EC use
- Little information is available for effects of UPA on breast feeding
  - *CDC recommends discarding breast milk for 24 hours after dosing*

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Screening and provision

- No clinical exam or pregnancy test necessary
- Pregnancy test if multiple episodes of unprotected intercourse have occurred earlier in month
  - *EC should NOT be withheld in order to test for pregnancy*
- Discuss possible side effects
- If no menses 3 weeks after taking EC, recommend pregnancy test
- Discuss need to abstain following UPA or LNG as these delay ovulation
- Use as an opportunity to discuss contraceptive plans

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Screening and provision

- IUDs can be safely placed same day with concurrent testing for gonorrhea and chlamydia
  - *Treat positive test results*
- IUDs are safe for adolescents and people who have not had a pregnancy

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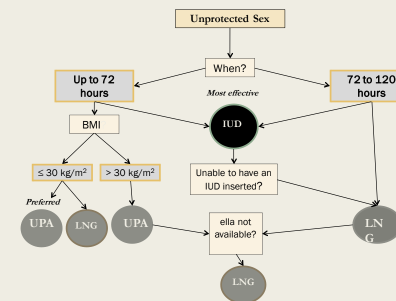

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Shared side effects of oral EC

- Most common side effects are headache (19%) and nausea (12%)[6]
- Fatigue, breast tenderness, lower abdominal pain, dizziness, and diarrhea have also been reported[8]

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Effects on mensural bleeding

- Irregular bleeding-menstrural cycle typically occurs within one week of expected time after single use
  - *16% of LNG users reported nonmenstrual bleeding in first week after use*[9]
- Menses can come early (11%) or late (28%) (*Contraceptive Technology*)

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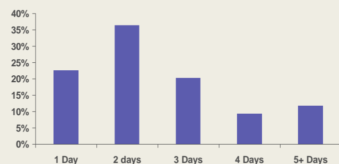
Effects on mensural bleeding



Spotting happens for 10-15% of people and can last up to 5 days

Ellertson C, Webb A, Blanchard K, Bigrigg A, Haskell S, Shochet T, Trussell J. Modifying the Yuzpe regimen of emergency contraception: a multicenter randomized controlled trial. Obstet Gynecol. 2003 Jun;101(6):1160-7. doi: 10.1016/s0029-7844(03)00353-3. PMID: 12798518.

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Obesity

- Levonorgestrel EC is less effective for those with BMI >25[10]
  - *A meta-analysis of oral EC studies demonstrated that the risk of pregnancy is one and one-half times greater in users with an overweight BMI (25–29.9 kg/m 2) and more than three times greater in users with an obese BMI (> 30 kg/m 2), compared to nonoverweight users*[12]
- Patients with overweight BMI have same failure rates as those with normal BMI for UPA use
  - *However, UPA ECP users with obesity are twice as likely to experience pregnancy compared to users with a normal BMI.*[12]
- Doubling the dose to 3mg not shown to improve effectiveness[13]
- Upper weight limit for effectiveness for LNG ~70kg while upper limit for UPA ~85kg

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Medication interactions with oral EC

- LNG and UPA are substrates of cytochrome P450
  - *Enzyme inducers may lower total dose of EC, therefore reducing effeteness*
  - *Clinical significance of these interactions is unclear*
- When taken with rifampin, UPA exposure is decreased 10-fold[14]
- UPA does not appear to decrease subsequent oral contraceptive pill efficacy.
  - *However, effectives of UPA is reduced by subsequent administration of oral contraceptive pills*
  - Administration of 75 mg desogestrel the day following UPA is associated with ovulation within five days in 45% of subjects, compared to 3% of subjects who took only UPA[15]
- SFP recommends delaying oral contraceptive initiation for 5 days following UPA

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American College of Obstetricians and Gynecologists recommendations

- Inform patients that copper IUD is the most effective option Prescribe UPA over LNG due to increased effectiveness
- Write advanced prescriptions to increase awareness
- Counsel about all contraceptive methods when seeing a patient for EC
- Counsel all women at risk for pregnancy on EC
- Provider referrals when appropriate
- Collaborate with pharmacies

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Patient case 1

Laura is a 24 yo cis-woman who is currently using the Nuvaring for contraception. She is sexually active with a cis-male partner and they do not use condoms.

Her roommate accidentally threw out her Nuvaring (it was in the shared refrigerator). She usually places a new ring on Sunday, but didn't notice that the ring was missing until Monday night, after the pharmacy was closed. Due to a busy work schedule, she did not make it to the pharmacy until Friday afternoon.

She and her partner had UPIC on Sunday and Wednesday that week.

Laura weighs 55kg and has no significant PMHx.

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Patient case 1

- Does Laura need EC?
- What type of EC would be best for Laura?
- At what point in the week did her Nuvaring become ineffective?

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Patient case 1

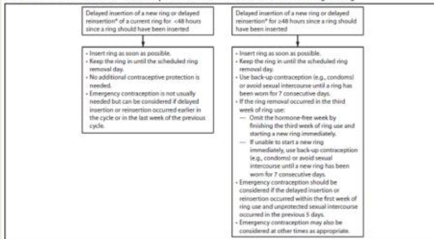
FIGURE 4. Recommended actions after delayed insertion or reinsertion with combined vaginal ring

Delayed insertion of a new ring or delayed reinsertion* of a current ring for <48 hours since a ring should have been inserted

- Insert ring as soon as possible.
- Keep the ring in until the scheduled ring removal day.
- No additional contraceptive protection is needed.
- Emergency contraception is not usually needed but can be considered if delayed insertion or reinsertion occurred earlier in the cycle or in the last week of the previous cycle.

Delayed insertion of a new ring or delayed reinsertion* for ≥48 hours since a ring should have been inserted

- Insert ring as soon as possible.
- Keep the ring in until the scheduled ring removal day.
- Use back-up contraception (e.g., condoms) or avoid sexual intercourse until a ring has been worn for 7 consecutive days.
- If the ring removal occurred in the third week of ring use:
  - Omit the hormone-free week by finishing the third week of ring use and starting a new ring immediately.
  - If unable to start a new ring immediately, use back-up contraception (e.g., condoms) or avoid sexual intercourse until a new ring has been worn for 7 consecutive days.
- Emergency contraception should be considered if the delayed insertion or reinsertion occurred within the first week of ring use and unprotected sexual intercourse occurred in the previous 5 days.
- Emergency contraception may also be considered at other times as appropriate.

* If removal takes place but the woman is unsure of how long the ring has been removed, consider the ring to have been removed for ≥48 hours since a ring should have been inserted or reinserted.

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Patient case 2

Ann is a 25 yo who presents to the office for well-woman exam. Her PMHx is significant for hypothyroidism, for which she is on levothyroxine daily, high blood pressure (recently diagnosed, no medications) and an elevated BMI of 47.

Her blood pressure in clinic today is 145/78

During the visit today, she endorses that she has been having frequent unprotected intercourse. Upon further questioning, she expresses that she does not desire to be pregnant at this time and is open to contraception options.

Can Ann be started on a method of birth control today?

Does she qualify for emergency contraception?

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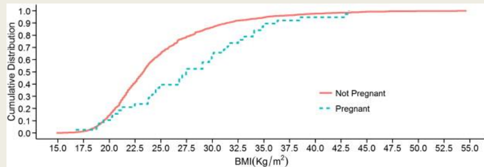
Patient case 2

Fig. 1. Cumulative frequency distribution of weight according to pregnancy status post-intake of LNG



Nathalie Kapp, Jean Louis Abitbol, Henri Mathé, Bruno Scherrer, Hélène Guillard, Erin Gainer, André Ulmann, Effect of body weight and BMI on the efficacy of levonorgestrel emergency contraception, Contraception, Volume 91, Issue 2, 2015, Pages 97-104,

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Patient case 2

Table 3. Pregnancy rate following LNG EC according to BMI categories.

	BMI (kg/m²)				
	< 20	20–25	25–30	30–35	≥ 35
N total	249	873	367	149	93
N pregnancies	4	11	9	10	4
Pregnancy rate	1.61%	1.26%	2.45%	6.71%	4.30%
95% CI[a]	0.44%–4.06%	0.63%–2.24%	1.12%–4.60%	3.26%–11.99%	1.18%–10.64%

Nathalie Kapp, Jean Louis Abitbol, Henri Mathé, Bruno Scherrer, Hélène Guillard, Erin Gainer, André Ulmann, Effect of body weight and BMI on the efficacy of levonorgestrel emergency contraception, Contraception, Volume 91, Issue 2, 2015, Pages 97-104,

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