Contraception for Women with Neurologic and Psychiatric Disorders

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Disclosures

- No financial disclosures
- Language - sometimes the term woman is used to denote biological sex, conflating gender with sex.

Objectives:

- Understand why addressing contraception is important, especially those with chronic medical conditions
- Describe the available contraceptive methods, including the benefits of long-acting reversible contraception (LARC)
- Discuss potential interactions between hormonal contraception and neurologic or psychiatric disease
- Evaluate for potential interactions between hormonal contraception and medications

Almost half of all pregnancies in the U.S. are unintended

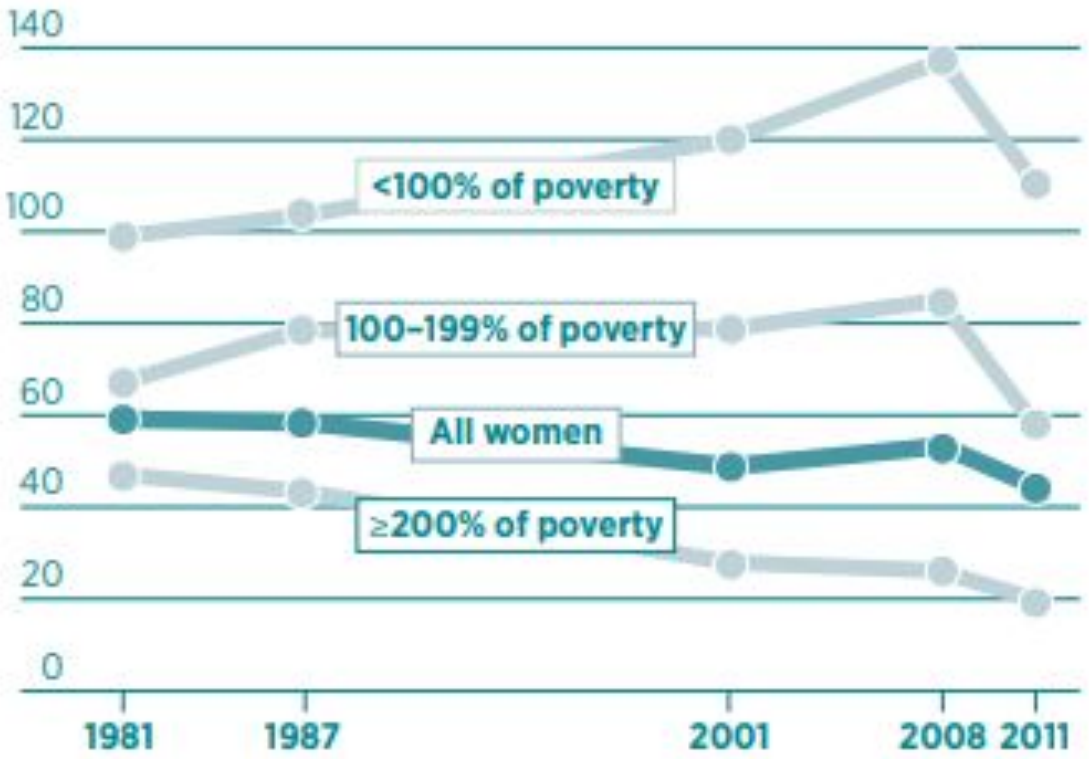
- 1 in 20 US women have an unintended pregnancy each year
- 46% pregnancies unintended, but only 18% “unwanted”
  - Significant proportion “wanted later”

Annual number of pregnancies in 2011= 6.1 million

Guttmacher Institute, 2019.

UNINTENDED PREGNANCY RATES

Unintended pregnancy is increasingly concentrated among low-income women.



Guttmacher Institute, 2019

› Perspect Sex Reprod Health. 2019 Mar;51(1):7-15. doi: 10.1363/psrh.12088. Epub 2019 Feb 14.

The Misclassification of Ambivalence in Pregnancy Intentions: A Mixed-Methods Analysis

Anu Manchikanti Gómez [1], Stephanie Arteaga [2], Elodia Villaseñor [3], Jennet Arcara [2], Bridget Freihart [4]

Journal of Midwifery & Women's Health

Review

Ambivalence Toward Pregnancy as an Indicator for Contraceptive Nonuse: A Systematic Review and Meta-Analysis

Allison LaCross[1,2], CNM, DNP, Arlene Smaldone[2,3], PhD, CPNP-PC, CDE, Jessica Angelson[4], CNM

Risks of unplanned pregnancy for patients with neurologic or psychiatric disease

- Some patients discontinue their medications- increasing risk of complications in pregnancy or from their disease
- Medical therapies may have teratogenic risk

Sub-optimal solutions:

- Prescription of inappropriate contraception may result in decreased method efficacy, increased risk of complications and/or impact on disease
- Patients denied contraceptives may rely on less effective methods

Knowledge of interactions and use of contraception by women with epilepsy (WWE)

Surveys of WWE at an academic clinic:

- 65% did not know their prescribed AED might interact with oral contraceptives
- Less than half knew of the potential for AED-related birth defects
- Only 53% reported using a moderately or highly effective method of contraception
- 21% reported withdrawal as primary method

Pack A et al. Epilepsy and behavior 2009;14:640-4.
Davis AR et al. Contraception 2008; 77:405-9.

Contraceptive options

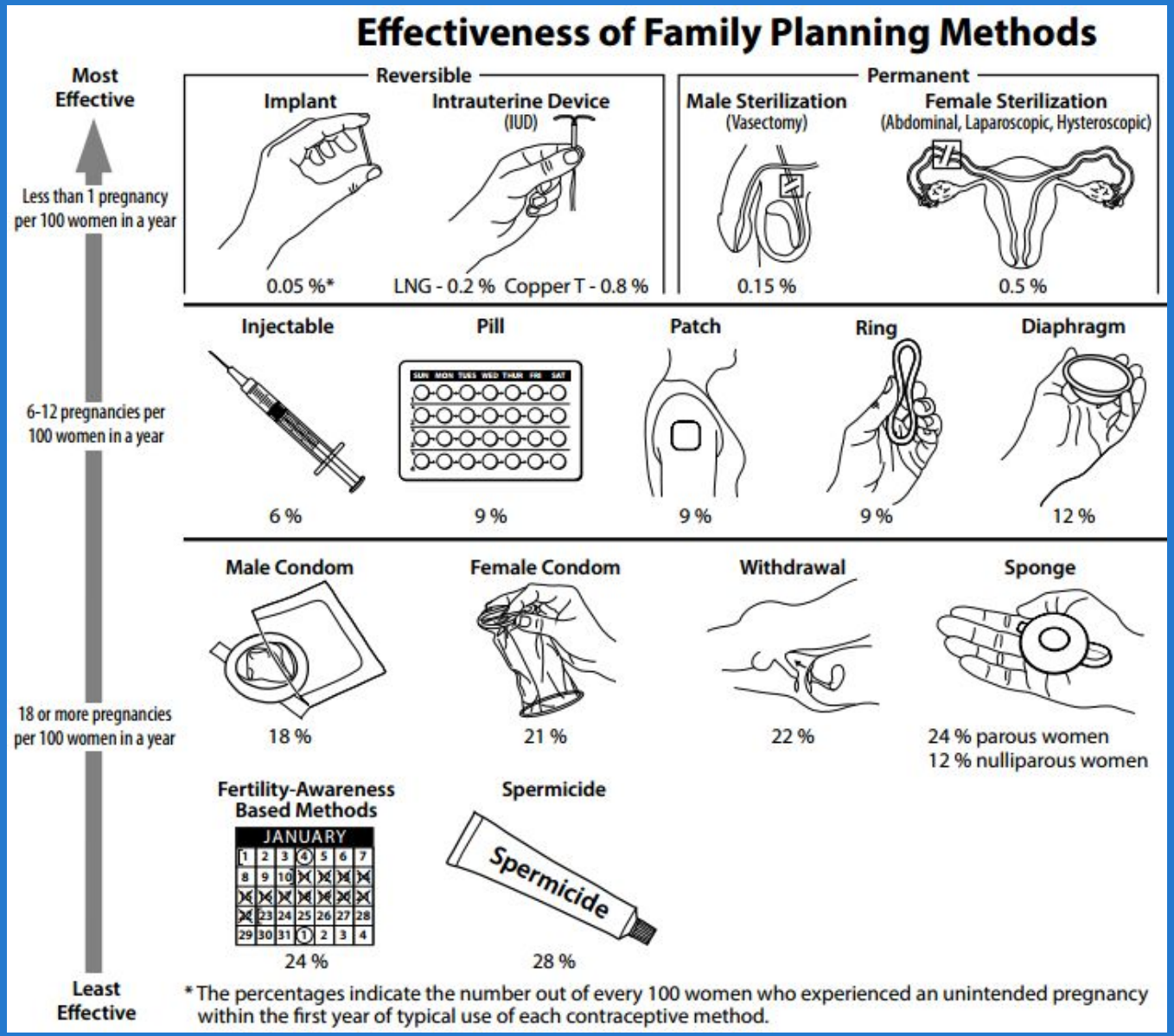
Method failure rates: % experiencing unintended pregnancy and % discontinuing in the first year

Method	Typical use	Perfect use	Discontinuation
No method	85	85	
Diaphragm	16	6	43
Condom (male)	15	2	57
OCP, patch, ring	8	0.3	33
DMPA (Depo)	3	0.3	44
IUD: Copper T	0.8	0.6	22
IUD: LNG-IUS	0.1	0.1	20
Subdermal implant	0.05	0.05	16
Female sterilization	0.5	0.5	0
Male sterilization	0.15	0.10	0

Trussell J. Contraceptive Efficacy. In: Hatcher et.al. Contraceptive Technology 20th edition, 2011

Contraceptive options and efficacy

LARC = long acting reversible contraception

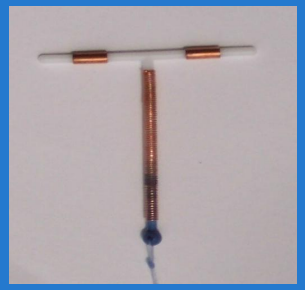


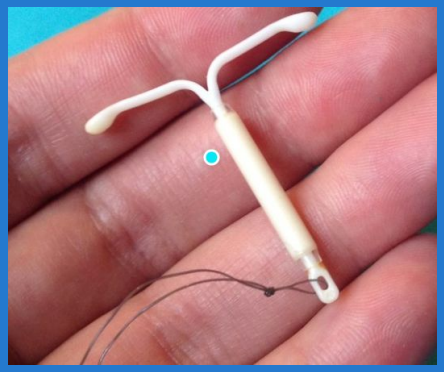
Intrauterine contraceptive devices available in the United States

Copper T 380A IUD

Paragard®

12 yrs of use
Menses - 1 day longer
50% heavier





Levonorgestrel (LNG) IUD

Mirena® & Liletta IUS
52 mg – LNG
20 mcg levonorgestrel /day
8 yrs of use
20% amenorrhea at 1 year (15-35% ovulatory cycles)
32 x 32 mm
Inserter – 4.4 mm

Kyleena® IUS
19.5 mg
17.5 mcg levonorgestrel /day
5 yrs of use
12% amenorrhea at 1 year (98%+ ovulatory)
28 x 30 mm
Inserter – 3.8 mm

Skyla® IUS
13.5 mg
6 mcg levonorgestrel /day
3 years use
28 x 30 mm

Data source: Mirena, Kyleena, Skyla prescribing information. Bayer Healthcare.

Implantable contraception available in the United States

<u>Etonogestrel Implant</u>
(Nexplanon ™)

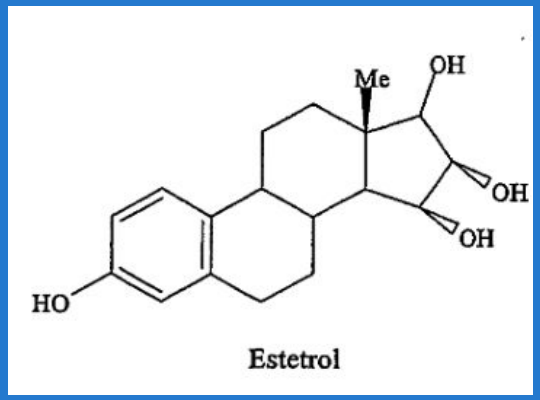
- **5 years of use**
- **Office insertion/removal**
- **Lower dose/lower side effect profile compared to DMPA (injection)**

- **Ovulatory inhibition**

New(er) Contraceptives

Slynd

- Drospirenone only oral contraceptive pill
- 4 mg drospirenone qd
- No estrogen, + ovulation suppression (!)



Estetrol

Annovera

- ethinyl estradiol/segesterone
- Yearly vaginal ring

Nexstellis

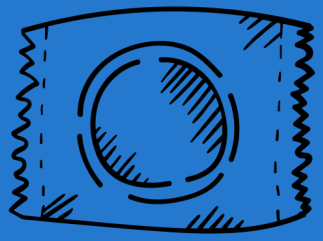
- Estetrol (E4) - Drospirenone
- Different side effect profile due to ER subtype binding affinities

OTC Contraceptive pills!

- Progestin-only pill
- 75 mcg norgestrel
  - more androgenicity than norethindrone
- ~ $15/month
- 98% efficacy perfect use
  - 91% typical

Non-Hormonal Contraception

- Barrier methods
- Spermicides & Vaginal Suppositories
  - Phexxi (lactic acid)
- Fertility awareness method
- Lactational amenorrhea
- Withdrawal
- Sterilization
  - male and female



How does hormonal contraception interact with neurologic disease?

- Headache disorders, including migraines
- Multiple Sclerosis
- Epilepsy
- Mood disorders

Contraception and headache disorders

- Is combined hormonal contraception (CHC) or HRT *safe* for women with migraine?
  - Major concern is stroke
- Does CHC *affect the clinical course* of migraine, or of other headache disorders?

Venous thromboembolism (VTE) risk with combined hormonal contraception alone

- Risk increases with increasing dose of estrogen (20-50 mcg ethinyl estradiol), age, smoking status
- VTE risk by type of progestin - modulator of estrogen risk?
- VTE risk related to patch or ring- higher overall estrogen exposure; for low-risk users no contraindication to initiation

So what are the absolute risks of stroke in women?

	Incidence	Risk ratio
Women (w/o migraine) **(Age 20 ; 40)**	**13/100,000** **2 ; 11/100,000**	**1.0**
w/migraine **(Age 20; 40)**	**17/100,000** **8;70/100,000**	**1.6**
w/migraine w/aura	**52/100,000**	**2.9**
w/ 30-35 mcg EE COC	**26/100,000**	**1.8**
w/ 50 mcg EE COC	**45/100,000**	**4.9**
w/ migraine and 50 mcg EE COC	**78/100,000**	**5.9**
w/migraine and (any COC) and age 40	**140-280/100,000**	**6-12**

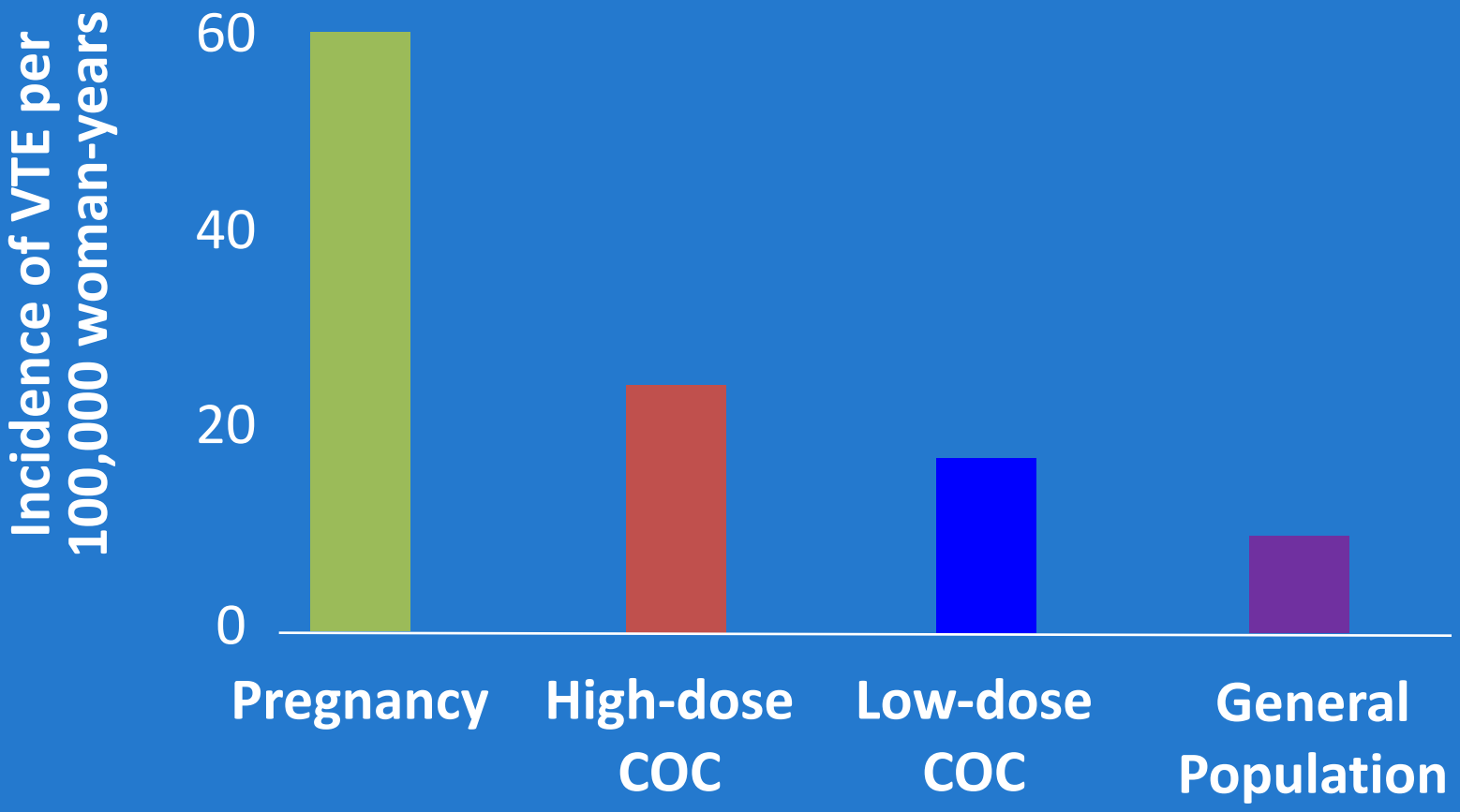
Risk of CVA with migraine +/- aura, +/- CHC

Case-control study of 25,887 women ages 15-49 with ischemic stroke (incidence 11/100,000 females)

	odds ratio (95% CI)
Migraine + aura + CHC	**6.1** (3.1-12.1)
Migraine + aura (no CHC)	**2.7** (1.9-3.7) Migraine + CHC (no aura) **2.2** (1.9-2.7)
Migraine (no aura, no CHC)	**1.8** (1.1-2.9)
No migraine + CHC	**1.4** (1.2-1.7)
No migraine, no CHC	reference

Champaloux et al. Am J Obstet Gyn, 2017

Comparative Risks of VTE



Shulman LP. J Reprod Med. 2003.
Chang J. In: Surveillance Summaries. 2003.

Use of combined hormonal contraception and stroke: A case-control study of the impact of migraine type and estrogen dose on ischemic stroke risk

Pelin Batur MD[1] | Meng Yao BS, MS[2] | Julia Bucklan DO[3] | Payal Soni MD[3] | Aarushi Suneja MD[4] | Ruth Farrell MD, MA[5] | Maryann Mays MD[3]

Headache, 2023

How do COCs affect the clinical course of migraine?

- Retrospective studies in headache clinics: COCs may worsen severity and frequency of headaches, cause new onset headache- but many design flaws
- Migraine with aura patients much more likely to worsen on COC compared to migraine without aura group
- Limited evidence that progesterone-only pills (desogestrel) may decrease severity of migraine +/- aura

Granella, Cephalagia, 2000; Sacco J Headache Pain 2018

Hormonal contraception to *treat* menstrual migraine

- Retrospective and prospective studies suggest reduction in menstrually-related migraine
  - Monophasic pill, vaginal ring, subdermal implant
  - LNG-IUD may not work due to breakthrough ovulation
- Use continuously - skip placebo pills
- Goal is to eliminate the culprit—estrogen withdrawal

Calhoun, *Headache* 2012; De Leo Fertil Steril 2011; Macias et al, *J Obstet Gynaecol* 2013;Nappi et al, *Contraception* 2013

Erenumab in menstrually-related migraines

Change From Baseline in Mean Monthly Migraine Days by Hormonal Contraception Status

	Received Hormonal Contraception			Did Not Receive Hormonal Contraception		
	Placebo ***N*** **= 20**	**Erenumab 70 mg** ***N*** **= 18**	**Erenumab 140 mg** ***N*** **= 27**	**Placebo** ***N*** **= 63**	**Erenumab 70 mg** ***N*** **= 50**	**Erenumab 140 mg** ***N*** **= 54**
Monthly migraine days at baseline, mean (SD)	9.5 (3.0)	8.5 (2.7)	8.9 (2.2)	8.3 (2.8)	8.2 (2.3)	8.2 (2.4)
Change from baseline over months 4–6, LSM (95% CI)	−1.6 (− 3.4, 0.25)	− 2.9 (− 4.8, − 1.0)	− 3.9 (− 5.5, − 2.4)	− 1.4 (− 2.2, − 0.6)	−3.3 (− 4.2, − 2.4)	−3.4 (− 4.2, − 2.5)
Difference from placebo		−1.3 (− 3.9, 1.2)	− 2.4 (− 4.7, − 0.1)		−2.0 (− 3.1, − 0.8)	−2.0 (− 3.1, − 0.8)
		P = 0.3	*P* = 0.045		*P* = 0.001	*P* < 0.001
Treatment by subgroup interaction *P* value over months 4–6	0.76					

Pavlovic, Jelena M., et al. "Efficacy and safety of erenumab in women with a history of menstrual migraine." *The journal of headache and pain* 21.1 (2020): 1-9.

How do new HA treatments interact w/ hormonal contraception?

- Study of CGRP antagonist (remigepant) on COC pharmacokinetics
- Modest increases in EE/NGM
  - AUC and maximum observed concentration
- Unlikely to negatively impact contraceptive effect or have significant health effects
- Similar results for other DDI studies (atogepant, ubrogepant)

Bjardwaj et al. Headache, 2023.

Observations: Headache and COCs

- More common in women 35 and older
- No effect from type or dose of progesterone
- Switching to lower dose COC may not improve headaches
  - 30 vs 20 EE: No diff in dropout due to HA.[1]
- If HA occurs in 1st cycle on COC, only 1/3 chance it will occur in 2nd cycle [4]

1 Bassol,Cephalalgia,2000
2 Edelman, Hum Reprod, 2006
3 Gerais, Int J Gynaecol Obstet, 1983
4 Berger, Contraception, 1979

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 65 / No. 3
July 29, 2016

U.S. Medical Eligibility Criteria for Contraceptive Use, 2016

https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6503.pdf

Criteria for method use based on best available evidence

1 No restriction (method can be used)

2 Advantages generally outweigh theoretical or proven risks

3 Theoretical or proven risks usually outweigh the advantages

4 Unacceptable health risk (method not to be used)

The CDC MEC chart: summary of recommendations for women with headaches

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Headaches	a) Nonmigraine (mild or severe)	1		1		1		1		1		1*	
	b) Migraine												
	i) Without aura (includes menstrual migraine)	1		1		1		1		1		2*	
	ii) With aura	1		1		1		1		1		4*	

1 **No restriction (method can be used)**

2 **Advantages generally outweigh theoretical or proven risks**

3 **Theoretical or proven risks usually outweigh the advantages**

4 **Unacceptable health risk (method not to be used)**

Summary for CHC:
1 = Non-migrainous HA
2 = Migraine w/o aura
4 = Migraines w/ aura ANY age
Or w/aura developing after CHC initiation

Contraception: effect on multiple sclerosis

Theoretical concern exists:

- MS relapse and exacerbations occur during pregnancy and postpartum period

Immune function fluctuations throughout the menstrual cycle

- RA, MS, SLE all fluctuate with monthly cycles and in menopause
- Estrogen suppresses T-cell dependent inflammation in MS and RA

Studies of Hormonal Contraception and incidence of MS

Oxford FPA Study (1968-1974)
- Women using CHC had a lower incidence of MS onset
- No associations between MS onset, duration of CHC use, or elapsed time since CHC use ended

BJOG 1998
- Prospective study of 46,000 CHC users
- Found no effect on MS incidence or survival

CDC Systematic review 2016
- 111 articles, 4 studies all suggested OCs do not affect disease course

Systematic Review & Meta Analysis 2022 (Ghajarzadeh et al, Int J Prev Med) - OCP use has no effect on development of MS

Concern about MS development or disease severity should not affect contraceptive choice

Villard-Mackintosh and Vessey. Contraception 1993
Thorogood and Hannaford. BrJ Obstet Gyn 1998, Hernan, et al. Neurology 2000

Other aspects of MS that may affect contraceptive choice

- Immobility and VTE risk
  - If MS results in lower extremity paraparesis or paresthesias
  - Risk of VTE increases with increasing immobility
  - Patients with immobility should be counseled on increased risk with estrogen containing contraceptives.

- Patient ability to apply/place method (such as diaphragm, patch, ring)

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Multiple sclerosis	a) With prolonged immobility	1		1		1		2		1		3	
	b) Without prolonged immobility	1		1		1		2		1		1	

MULTIPLE SCLEROSIS JOURNAL | MSJ

Topical Review

Contraception for women with multiple sclerosis: Guidance for healthcare providers

Maria K Houtchens, Lauren B Zapata, Kathryn M Curtis and Maura K Whiteman

Therapeutic Advances in Neurological Disorders

Sex effects across the lifespan in women with multiple sclerosis

Kristen M. Krysko*, Jennifer S. Graves*, Ruth Dobson, Ayse Altintas, Maria Pia Amato, Jacqueline Bernard, Simona Bonavita, Riley Bove, Paola Cavalla, Marinella Clerico, Teresa Corona, Anisha Doshi, Yara Fragoso, Dina Jacobs, Vilija Jokubaitis, Doriana Landi, Gloria Llamosa, Erin E. Longbrake, Elisabeth Maillart, Monica Marta, Luciana Midaglia, Suma Shah, Mar Tintore, Anneke van der Walt, Rhonda Voskuhl, Yujie Wang, Rana K. Zabad, Burcu Zeydan, Maria Houtchens* and Kerstin Hellwig* on behalf of the International Women in MS (iWiMS)

Hormones and epilepsy

- Reproductive hormones may increase or decrease seizure threshold
  - *Estrogen → pro-convulsant*
  - *Progesterones → anti-epileptic*

- "Catamenial epilepsy": defined as a consistent doubling in seizure frequency in peri-menstrual, peri-ovulatory or luteal phase of cycle

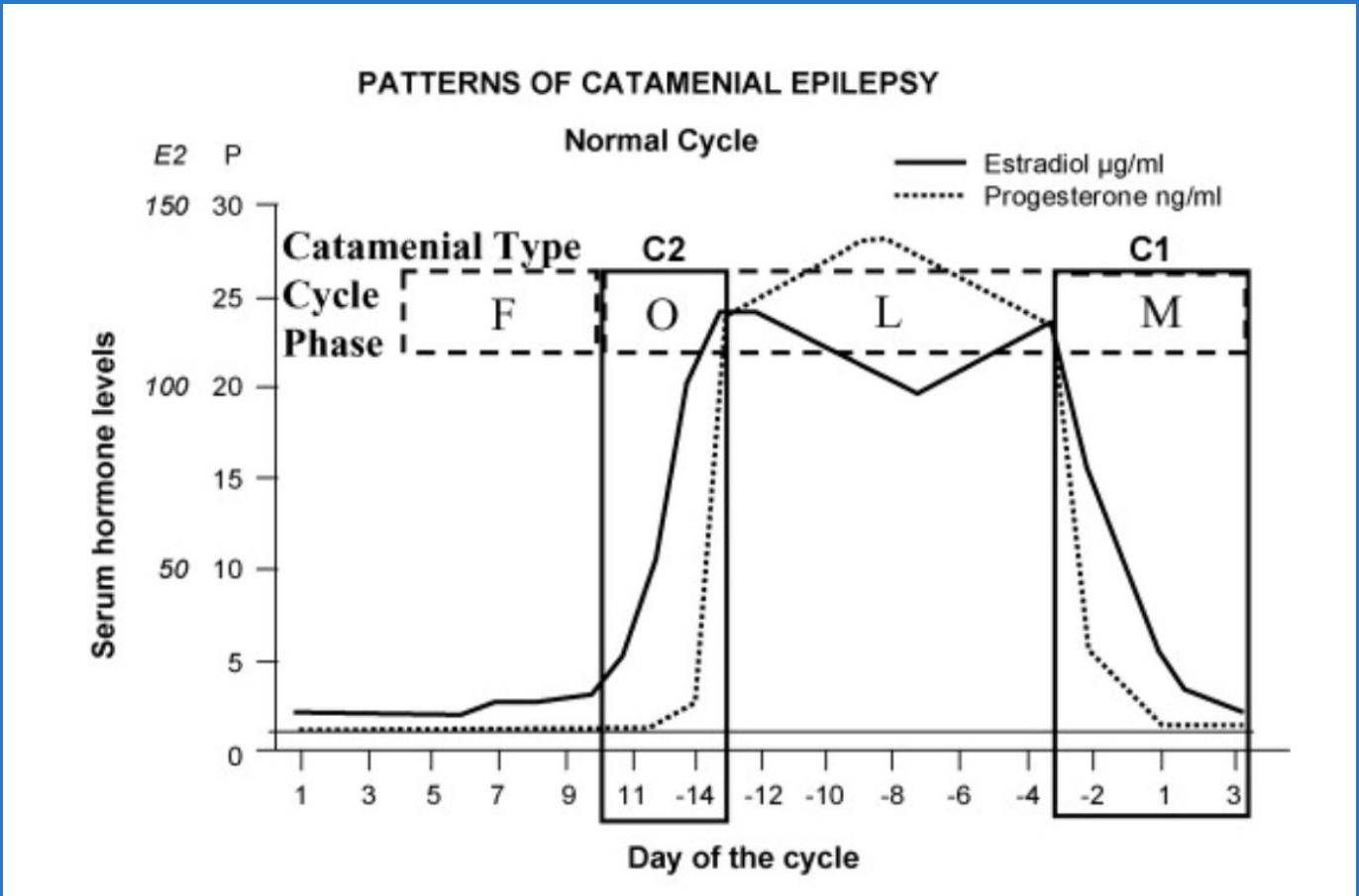
Harden CL and Pennell PB. Lancet 2013; 12:72-83.

Contraception: effect on epilepsy

- Initiation or ongoing use of combined oral contraceptives (COCs) does not change incidence of epilepsy; COCs may impact seizure type or frequency
- Exogenous hormones may increase or decrease seizure threshold, 70-92% of WWE report no change
- Menstrual suppression is a reasonable approach for any WWE, even if seizure pattern not clearly linked to same time point in cycle

Beier 2018; Davis et al. 2014, in Contraception for the Medically Challenging Patient

Catamenial Epilepsy



Herzog, Andrew G. "Catamenial epilepsy: definition, prevalence pathophysiology and treatment." *Seizure* 17.2 (2008): 151-159.

CDC MEC guidelines for epilepsy

Condition	Sub-Condition	CHC		POP		Injection		Implant		LNG-IUD		Cu-IUD	
		I	C	I	C	I	C	I	C	I	C	I	C
Endometrial cancer[†]		1		1		1		1		4	2	4	2
Endometrial hyperplasia		1		1		1		1		1		1	
Endometriosis		1		1		1		1		1		2	
Epilepsy[†]	*(see also Drug Interactions)*	1*		1*		1*		1*		1		1	
Gallbladder disease	a) Symptomatic												
	i) treated by cholecystectomy	2		2		2		2		2		1	

Legend:

1	No restriction (*method can be used*)	**3**	Theoretical or proven risks usually outweigh the advantages
2	Advantages generally outweigh theoretical or proven risks	**4**	Unacceptable health risk (*method not to be used*)

Patients want their neurologists to bring up SRH, contraception

"I do wish that conversations with my doctors… [included] women's health and epilepsy because I really wanna find that out… I want to know beforehand… I don't want to be dumbfounded and be like, is this gonna affect my seizures now? I would love for more of my doctors to have conversations about women's health and epilepsy."

"I feel like it's the doctor's part to give them the knowledge or suggest the knowledge to them because a lot of people aren't aware of the questions they should be asking with their own health issues."

Kirkpatrick, Laura, et al. "Preferences and experiences of women with epilepsy regarding sexual and reproductive healthcare provision." *Epilepsy & Behavior* 129 (2022): 108631.

Case Study

JG, 28-year-old G0
Epilepsy since age 13
Current medications:
- lamotrigine (Lamictal)
- carbamazepine (Tegretol)

Relevant GYN Hx:
Currently using condoms, had excessive breakthrough bleeding with prior COC use- told that she "can't take birth control"
No current plans for pregnancy

Hormonal Contraception Interacts with Some Anti-Epileptic drugs (AEDs)

- AEDs and steroid hormones are both substrates of the CYP3A4 system in the liver; certain AEDs will induce metabolism and increase clearance of hormones

- In addition, unique interaction exists with lamotrigine (LTG) hormonal contraceptives containing estrogen will increase LTG metabolism

Dutton and Foldvary-Schaefer. Int Rev Neurobiol 2008;83:113-34.

AEDs by Enzyme Inducing Status

INDUCERS

- Carbamazepine
- Felbamate
- Oxcarbazepine
- Phenobarbital
- Phenytoin
- Primidone
- Rufinamide

NON-INDUCERS

- Clobazam
- Clonazepam
- Ethosuximide
- Ezogabineb
- Gabapentin
- Lacosamide
- Levetiracetam
- Pregabalin
- Tiagabine
- Valproate
- Vigabatrin
- Zonisamide

UNIQUE INTERACTIONS

Lamotrigine* Topiramate**

Contents lists available at ScienceDirect

Contraception

journal homepage: www.elsevier.com/locate/contraception

Original Research Article

Real-world effect of a potential drug-drug interaction between topiramate and oral contraceptives on unintended pregnancy outcomes ☆,☆☆

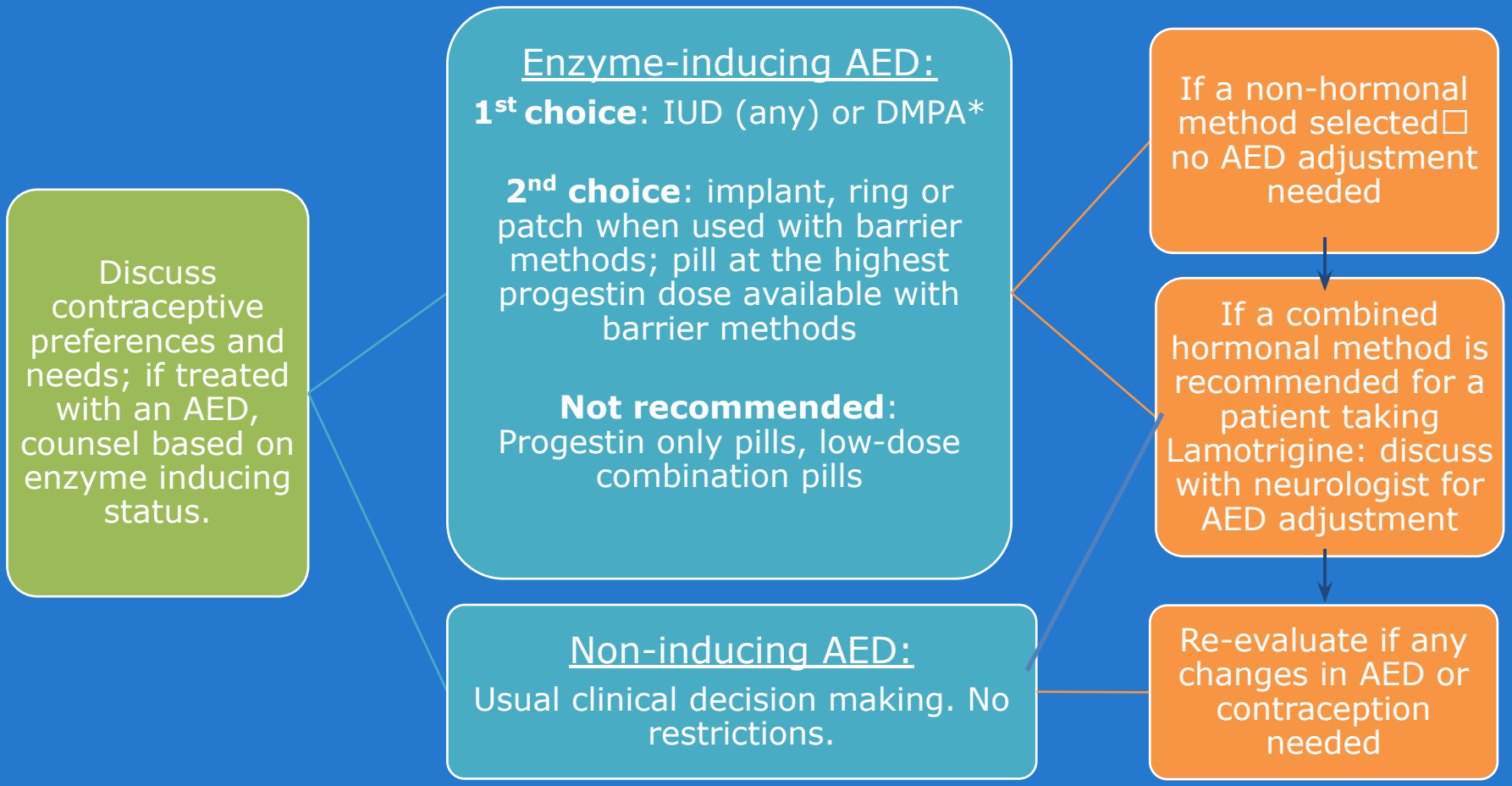
Amir Sarayani [a,b], Almut Winterstein [a,b], Rodrigo Cristofoletti [c,d], Valva Vozmediano [c,d], Stephan Schmidt [c,d], Joshua Brown [a,b,*]

- Retrospective cohort study of patients using topiramate for headache suppression vs using another medication for headache suppression, using OCPs, following patients for up to 1 year and measuring rates of pregnancy
- No increased rate of pregnancy in the topiramate group
- Recent study on etonogestrel (nexplanon) showed negative impact on levels that could lead to breakthrough ovulation

Contraception, 2023

Larowitz et al, Obstetrics & Gynecology, 2022

Recommending Contraception for WWE



Adapted from Davis et al. 2014, in Contraception for the Medically Challenging Patient

Table 1 Contraceptive drug interactions and teratogenic effects of antiseizure medications

Medication	Levels reduced by estrogen-containing contraception[a]	May affect hormonal contraceptive efficacy[b]	Teratogenicity[c] (% major congenital malformations)
Lamotrigine	Yes	Mixed evidence for effect at daily doses of 300 mg or more	Within background rate[d] (2.9%)
Levetiracetam	No	No	Within background rate (2.8%)
Topiramate	No	At daily doses of 200 mg or more	3.9%
Valproic acid	Yes	No	10.3%
Phenobarbital	No	Yes	6.5%
Phenytoin	No	Yes	6.4%
Carbamazepine	No	Yes	5.5%
Oxcarbazepine	No	At daily doses of 1,200 mg or more	Within background rate (3.0%)

[a]Includes combined oral contraceptive pills, contraceptive patch, and vaginal ring.
[b]Includes combined oral contraceptive pills, progesterone-only contraceptive pills, contraceptive patch, vaginal ring, etonogestrel intradermal implant.
[c]Based on data from the EURAP study. Note that teratogenicity varied by dose for certain medications. For example, lamotrigine at daily doses of 325 mg or more carried a 4.3% risk of major congenital malformations (which is above the background rate).[14]
[d]Background rate of major congenital malformations in pregnancy is 2–3%.[14]

Kirkpatrick et al., Preventative Approaches in Women's Neurology, 2022

Counseling WWE on Contraceptive Options

- Myth-busting: clarify that hormonal contraception is safe and appropriate for many WWE

- Common questions and concerns:
  - IUDs can safely be used in nulliparous women and in WWE requiring MRI for brain imaging
  - Unscheduled bleeding shouldn't be a trigger for seizure, also not correlated with inadequate efficacy
  - Emergency contraception is safe, though unknown efficacy in setting of eiAEDs

Davis et al. 2014, in Contraception for the Medically Challenging Patient

How does hormonal contraception interact with psychiatric disease?

- Depression
- Anxiety
- PMDD
- Other disorders

→ Does HC result in higher risk of developing a mood disorder?

→ Does initiation of HC impact mood in women with previous diagnosis of depression or anxiety?

Does HC increase incidence of depression?

- Mood symptoms are a commonly reported reason for method discontinuation
- Many prior studies have had contradictory results
- National Longitudinal Study of Adolescent Health: sexually active women ages 25-35 using HC had lower mean scores of depressive symptoms compared to women using non-hormonal or no method

Keyes et al., Am J Epidemiol 2013

WELL | LIVE

Contraceptives Tied to Depression Risk

By NICHOLAS

shots HEALTH NEWS FROM NPR

YOUR HEALTH

Does Some Birth Control Raise Depression Risk? That's Complicated

October 9, 2016 · 2:40 PM ET

TARA HAELLE

The Washington Post

'It's not in your head': Striking new study links birth control to depression

Research

JAMA Psychiatry | Original Investigation

Association of Hormonal Contraception With Depression

Charlotte Wessel Skovlund, MSc; Lina Steinrud Mørch, PhD; Lars Vedel Kessing, MD, DMSc; Øjvind Lidegaard, MD, DMSc

IMPORTANCE Millions of women worldwide use hormonal contraception. Despite the clinical evidence of an influence of hormonal contraception on some women's mood, associations between the use of hormonal contraception and mood disturbances remain inadequately addressed.

OBJECTIVE To investigate whether the use of hormonal contraception is positively associated with subsequent use of antidepressants and a diagnosis of depression at a psychiatric hospital.

+ Supplemental content

+ CME Quiz at jamanetworkcme.com and CME Questions page 1208


Research

JAMA Psychiatry | Original Investigation

Association of Hormonal Contraception With Depression

Charlotte Wessel Skovlund, MSc; Lina Steinrud Mørch, PhD; Lars Vedel Kessing, MD, DMSc; Øjvind Lidegaard, MD, DMSc

N= 1,061,997 Danish women ages 15-34 (1995-2013)

- Increased RR for first use of an anti-depressant following HC use compared to non-users
  - OCPs 1.23 (1.22-1.25)
  - POPs 1.34 (1.27-1.43)
  - Patch 2.0 (1.76-2.18)
  - Ring 1.6 (1.55-1.69)
  - LNG IUD 1.4 (1.31-1.42)

Incidence rate = 2.2 per 100 women-years with HC, compared to 1.7 per 100 women-years in non-users

Therefore, ABSOLUTE RISK is small (0.5 additional women per 100-women-years)

Association of Hormonal Contraception With Suicide Attempts and Suicides

Charlotte Wessel Skovlund, Ph.D., Lina Steinrud Mørch, Ph.D., Lars Vedel Kessing, D.M.Sc., Theis Lange, Ph.D., Øjvind Lidegaard, D.M.Sc.

N= 475,802 Danish women entered study at age 15 (1996-2013)

- Increased RR for first suicide attempt following initiation of HC use compared to non-users = 1.97 (95% CI 1.85-2.10)

- Increased RR of suicide following initiation of HC compared to non-users = 3.08 (95% CI 1.34, 7.08)

ABSOLUTE RISKS

- 14 suicide attempts per 10,000 woman-years
- 0.12 suicides per 10,000 woman-years

Does HC worsen disease for women with depression or bipolar disease?

- CDC systematic review, December 2016: 2376 articles identified, only SIX met inclusion criteria (use of a validated screening instrument)
  - OC, LNG-IUD and DMPA use not associated with worse clinical course of disease compared to no hormonal contraception

- Joffe et al, 2003- premenstrual mood not impacted by OCPs
  - Only predictor was prior major depression– OCP use may cause worsening of premenstrual mood (OR = 2.0)
  - Predictor of improving premenstrual mood was PMDD or dysmenorrhea

Pagano, HP et al. Contraception 2016
Joffe H et al. Am J Obstet Gynecol 2003

Additional studies on HC and depression

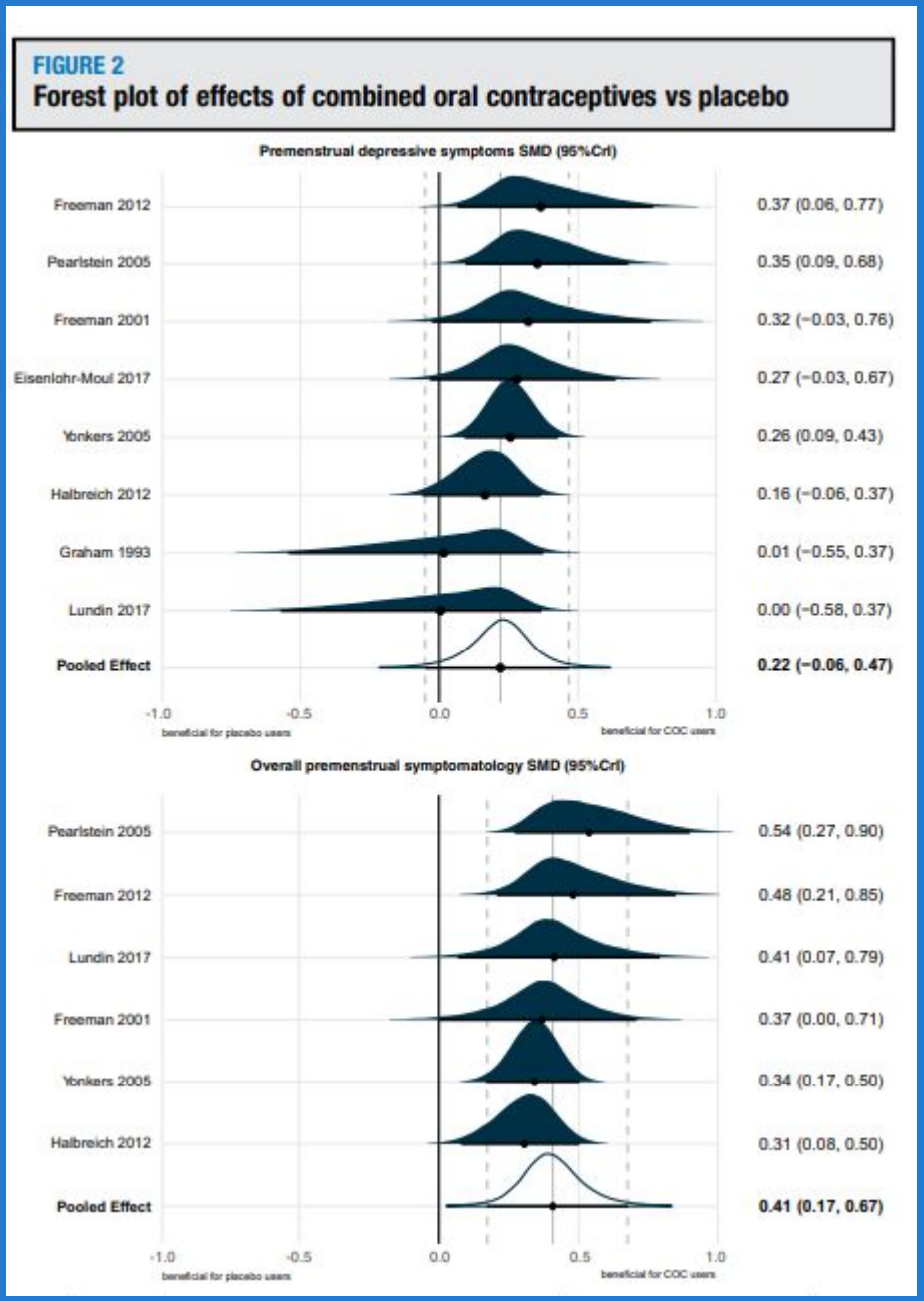
- Large retrospective study of postpartum women on hormonal contraception (n=75,528) majority of methods -minimal difference in rates of depression compared to non-users.[1]
- Systematic review of progestin-only contraception: "Despite perceptions in the community of increased depression following the initiation of progestin contraceptives, the preponderance of evidence does not support an association based on validated measures." [3]
- Swedish cohort study: ~ 740,000 pts, 15-25 years of age, no increased risk of depression w/ COC/POP.

1. *Roberts TA and Hanson S. Contraception 2017. 2. Zettermark et al. PLoS One 2018. 3. Worly B et al. Contraception. 2018. 4 Lundin C and Witman A et al. BJOG 2022.*

› Front Endocrinol (Lausanne). 2022 Mar 11;13:799675. doi: 10.3389/fendo.2022.799675. eCollection 2022.

The Impact of Hormonal Contraceptive Use on Serotonergic Neurotransmission and Antidepressant Treatment Response: Results From the NeuroPharm 1 Study

Søren Vinther Larsen [1 2], Brice Ozenne [1 3], Kristin Köhler-Forsberg [1 2 4], Asbjørn Seenithamby Poulsen [1], Vibeke Høyrup Dam [1], Claus Svarer [1], Gitte Moos Knudsen [1 2], Martin Balslev Jørgensen [4], Vibe Gedso Frokjaer [1 2 4]



de Wit, Anouk E., et al. "Efficacy of combined oral contraceptives for depressive symptoms and overall symptomatology in premenstrual syndrome: pairwise and network meta-analysis of randomized trials." *American journal of obstetrics and gynecology* 225.6 (2021): 624-633.

MEC guidelines for depression

Condition	Sub-Condition	CHC		POP		Injection		Implant		LNG-IUD		Cu-IUD	
		I	C	I	C	I	C	I	C	I	C	I	C
Depressive disorders		1*		1*		1*		1*		1*		1*	

Specific to combined hormonal

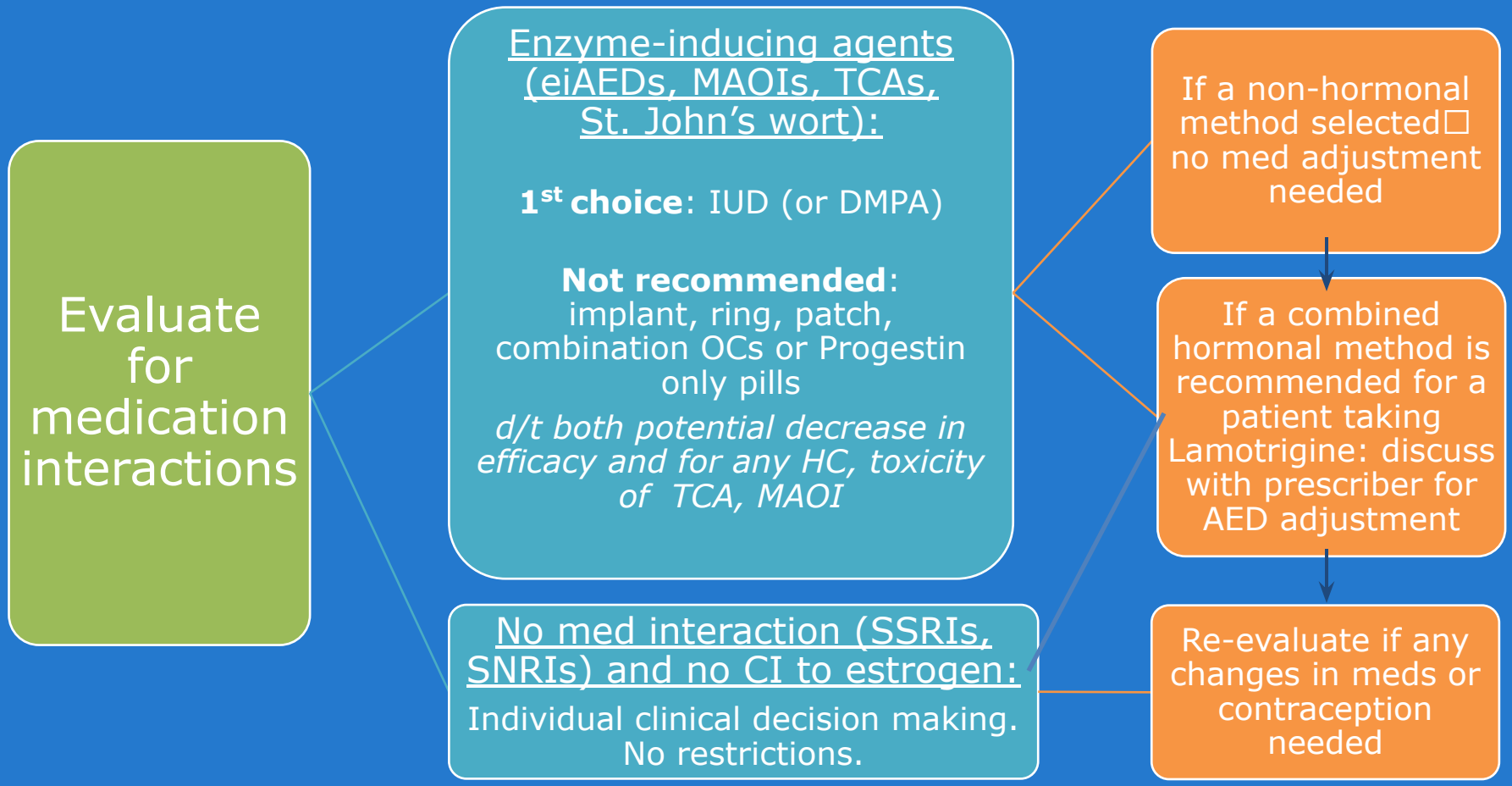
1

Clarification: If a woman is receiving psychotropic medications or St. John's wort, see Drug Interactions section.

Evidence: COC use was not associated with increased depressive symptoms in women with depression or scoring above threshold levels on a validated depression screening instrument compared with baseline or with nonusers with depression. One small study of women with bipolar disorder found that oral contraceptives did not significantly change mood across the menstrual cycle (*207*).

Consensus opinion: No change to initial contraceptive decision making indicated

Recommending Contraception for Women with Depression and/or Anxiety



Adapted from Contraception for the Medically Challenging Patient, 2014

Recommending Contraception for Women with Depression and/or Anxiety

Discuss contraceptive preferences and needs; counsel based on potential adherence, or mood side effect concerns

<u>For adherence concerns:</u>

1st choice: LARC or sterilization

2nd choice: DMPA, implant, ring or patch

EC as back-up

Not optimal:

COCs (daily)

Not recommended:

Progestin only pills

<u>Mood side effect concerns:</u>

Reversible, low-dose or non-hormonal methods. Consider continuous dosing or extended cycle options.

<u>PMDD</u>

Most HC will improve symptoms, esp. extended cycle or continuous. Drospirenone COCs approved for treatment

<u>Postpartum contraception</u>

All methods acceptable- minimize estrogen < 3 mo d/t VTE risk

Adapted from <u>Contraception for the Medically Challenging Patient</u>, 2014

When seeing a reproductive age woman, consider adding this routine screening…

Would you like to become pregnant in the next year?

www.onekeyquestion.org

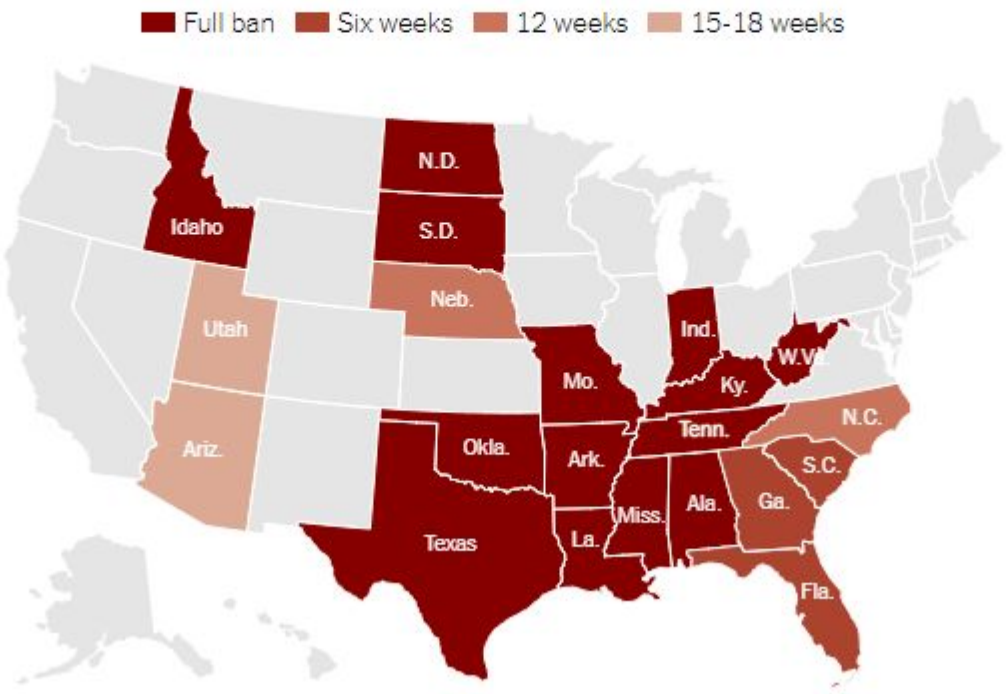
What if Contraception Fails?

- Nearly 1 million abortions in the US in 2020
  - 1 in 5 pregnancies end in abortion
- 92% in the first trimester
  - Aspiration
  - > 50% Medication abortion (up to 11 weeks GA)

Guttmacher, 2022:
https://www.guttmacher.org/article/2022/06/long-term-decline-us-abortions-reverses-showing-rising-need-abortion-supreme-court

Tracking Abortion Bans Across the Country

By The New York Times Updated May 1, 4:40 P.M. ET



Federal judge in Texas suspends FDA approval of abortion pill

> The ruling from U.S. District Judge Matthew Kacsmaryk in Amarillo could potentially upend access to medication abortion nationwide.

BY **ELEANOR KLIBANOFF** APRIL 7, 2023 UPDATED: 8 PM CENTRAL

LAW

Supreme Court blocks lower court decision in case on FDA approval of abortion pill

April 21, 2023 · 6:59 PM ET

Nina Totenberg

Drugmakers sign letter supporting FDA and calling for reversal of Texas judge's mifepristone ruling

By Carma Hassan, CNN

Published 3:12 PM EDT, Mon April 10, 2023

Summary

- Prevention of unplanned pregnancy can minimize both maternal and pregnancy complications; assess reproductive age women regularly for contraceptive need
- There are minimal impacts of hormonal contraception on neurologic and psychiatric disease- except for migraine disorders, and possibly mood disorders
- Potential for medication interactions is present- use available resources or refer for consultation