CONTRACEPTION CONUNDRUMS

Dr. Nicole Todd MD FRCSC
PCRM SYMPOSIUM
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DISCLOSURE

• Faculty: Nicole Todd
• Relationships with commercial interests:
  • Bayer – Received honoraria
• Employee of PHSA, VCH
  • Cross appointment within Department of Family Practice
• Off label medication list will be clearly marked with Asterix
DISCLOSURE – MITIGATING BIAS

• I will not be speaking on specific formulations of combined hormonal contraceptives, unless directly supported by research literature

OBJECTIVES

• Recommend safe contraceptive options based on SOGC, WHO and CDC MEC
• Review **UPDATES** in use of combined hormonal contraceptives (pill, patch, ring)
  • Post-partum, Headaches, Obesity, VTE Risk, Mood
• Dispel myths for contraception in **peri-menopause**
  • Recommend safe contraceptive options based on CDC (2016) and FSRH (2017) guidelines
## CDC MEDICAL ELIGIBILITY CRITERIA FOR CONTRACEPTIVE USE

<table>
<thead>
<tr>
<th>Category</th>
<th>Recommendation</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>A condition for which there is no restriction for the use of the contraceptive method</td>
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<tr>
<td>2</td>
<td>A condition for which the advantages of using the method generally outweigh the theoretical or proven risks</td>
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<tr>
<td>3</td>
<td>A condition for which the theoretical or proven risks usually outweigh the advantages of using the method</td>
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<tr>
<td>4</td>
<td>A condition that represents an unacceptable health risk if the contraceptive method is used. This method should not be used</td>
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</tbody>
</table>
CHC AND POSTPARTUM

- **Breastfeeding**
  - Recommend exclusive breastfeeding until 6 months, continuing to 1 year
  - <21 days PP = Category 4
  - 21-30 days PP = Category 3
    - Consider Category 4 if: age>35 yr, previous VTE, thrombophilia, transfusion at delivery, PPH, peripartum cardiomyopathy, BMI >30, post C/S, pre-eclampsia, smoking
  - 30-42 days PP = Category 2
    - Category 3 if risk factors: age>35 yr, previous VTE, thrombophilia, transfusion at delivery, PPH, peripartum cardiomyopathy, BMI >30, post C/S, pre-eclampsia, smoking
  - >42 days PP = Category 2

CDC, 2016, Appendix A

CHC, POSTPARTUM AND BREASTFEEDING

- Current evidence is conflicting regarding effects of COC on breastfeeding
  - Some low to fair quality studies demonstrated greater supplementation and decreased breastfeeding continuation in COC users
  - No consistent effect on infant growth, illness, health outcomes
    - Some low to fair quality studies demonstrated decreased infant weight gain if COC initiated in the first 6 weeks postpartum
  - **CDC 2016: discuss information regarding risks, benefits and alternatives in women who may be at risk for breastfeeding difficulties (previous history, medical conditions, perinatal complications, preterm delivery)**

CDC MEC, 2016
Tepper et al, 2015
CHC AND POST-PARTUM

- Not Breastfeeding
  - <21 days PP = Category 4
  - 21-42 days PP = Category 2
    - Consider Category 3 if: age>35 yr, previous VTE, thrombophilia, transfusion at delivery, PPH, peripartum cardiomyopathy, BMI >30, post C/S, pre-eclampsia, smoking
  - >42 days PP = Category 1

CDC, 2016, Appendix A

CONTRACEPTION POST-ABORTION

- CHC can be initiated within 7 days of first, and second trimester abortion, including immediately postabortion
- POPs can be started within 7 days, including immediately postabortion
- DMPA can be initiated within 7 days of abortion, including immediately postabortion
- IUD can be inserted immediately post-procedure for first and second trimester surgical abortion

NAF Guidelines 2018
CDC MEC 2016
CHC AND MIGRAINES

- CDC:
  - Migraines without aura = Category 2
  - Migraine with aura = Category 3
  - In presence of additional risk factors (cigarette smoking, HTN, obesity, history of cardiovascular disease, DVT, PE), **CHC should be avoided**
  - Preference to CHC <35 mcg EE
  - Additional thrombophilia screening, echo (patent foramen ovale), neuroimaging is not necessary
  - If migraine w/w/o aura develops during CHC initiation, suggest switch to progestin only option (pill, DMPA, LNG IUD), or non-hormonal option
  - Women with migraine w/w/o aura can safely use emergency contraception (LNG, ulipristal acetate, copper IUD)

CDC MEC, 2016
Sacco et al, 2107

CHC AND OBESITY

- One large cohort study demonstrated an increased pregnancy rate in obese COC users compared to non-obese users
  - However, larger cohort studies have not demonstrated an effect of BMI on COC efficacy
- Obese women have lower peak hormone levels
  - The hormone trough levels are similar between obese and non-obese users
  - Similar ovarian suppression
- SOGC: A small increase in contraceptive failure in women with BMI >30 cannot be excluded
  - However, blood pressure is the ONLY examination and/or investigation that is required prior to initiation
  - Consider Extended Cycle (84/7), or cyclic 24/4 regimens as they may have lower failure rates.

Black et al, 2017
**CHC AND VTE**

- Combined oral contraceptive users have 2-3X increase in VTE Risk
- The risk of VTE in the first year of COC use is higher than subsequent years
- Some retrospective and cohort studies have demonstrated increased risk of VTE in formulations with 3rd and 4th generation progestins
  - Prospective studies have NOT demonstrated increased risk of VTE associated with specific progestins
- **SOGC (2017): We should not alter prescribing practice based on progestin type**

References:
- Dinger J et al, 2014
- Black et al, 2017

**HISTORY OF VTE, NOT ON ANTICOAGULATION**

- High Risk for Recurrence (>1 risk factors)
  - Estrogen-associated VTE, Pregnancy associated VTE, idiopathic, known thrombophilia (including APAS), active cancer, recurrent VTE
  - **Category 1 – Copper IUD**
  - **Category 2 – LNG IUD, DMPA, POP**
  - **Category 4 - CHC**
- Lower Risk for Recurrence
  - No risk factors
  - **Category 1 – Copper IUD**
  - **Category 2 – LNG IUD, DMPA, POP**
  - **Category 3 - CHC**
VTE ON ANTICOAGULATION FOR > 3 MONTHS

- Menstrual suppression
  - Risk/benefit discussion with patient regarding use of CHC, if low risk of recurrence
  - Hemorrhagic cysts
  - Heavy menstrual bleeding
- IUD
  - Insertion of IUD does not pose significant bleeding risk
  - LNG IUD may be used for treatment of heavy menstrual bleeding for women on anticoagulation

PROGESTIN ONLY METHODS AND VTE

- POP does not increase VTE risk
- DMPA and VTE
  - Case control study (N=11 VTE) demonstrated VTE OR 2.19 (95% CI 0.66 to 7.26)\(^1\)
  - Case-control DMPA (N=47) demonstrated VTE OR 2.2 (95% CI 1.3 to 4)\(^2\)
  - Case-control DMPA (N=20) demonstrated VTE 3.6 (95% CI 1.8 to 7.1)\(^3\)
  - Meta-analysis for VTE in DMPA users demonstrated OR 2.67 (95% CI 1.29-5.53)\(^4\)
- Further high quality research is needed
- CDC (2016), WHO (2015) and SOGC (2016) do not consider VTE as a contraindication to DMPA use

\(^1\)WHO, 1998
\(^2\)Bergendal et al, 2014
\(^3\)van Hylckama et al, 2010
\(^4\)Mantha et al, 2012
CHC, DEPRESSION AND SUICIDE

- Large Danish cohort (1,061,997 women) demonstrated higher rate of first anti-depressant among COC users (RR 1.23, 95% CI 1.22-1.25)
  - This effect was higher amongst adolescents, and when compared to never users
  - Database study, whereby causation link cannot be attributed

- Large Danish cohort (475,802) demonstrated users of hormonal contraception had higher rate of suicide attempts and suicides (1.97, 95% CI 1.85-2.10, and 3.08, 95% CI 1.34-7.08 respectively)
  - This effect was higher amongst adolescents
  - Database study, whereby causation link cannot be attributed

References:
- Skovlund et al, 2017
- Skovlund et al, 2018
- Black et al, 2017

CHC, DEPRESSION, AND SUICIDE

- SOGC 2017: there are no high quality placebo controlled studies that demonstrated increased risk of mood changes
  - Discuss mood symptoms at initial and follow up visits, consider switching to another formulation if symptoms.

- SOGC 2017: Women with PMDD: may benefit from CHC containing drospirenone (Yaz, Yasmin)

References:
- Skovlund et al, 2017
- Skovlund et al, 2018
- Black et al, 2017
CONTRACEPTION BY AGE

NATIONAL SURVEY OF FAMILY GROWTH
• AGE IS A SIGNIFICANT PREDICTOR OF NONUSE OF CONTRACEPTION
• 24% OF 40-44 YEAR OLDS WERE NOT USING CONTRACEPTION
• LOWER PERCEIVED RISK OF PREGNANCY

<table>
<thead>
<tr>
<th>Age group (20-24 = reference group)</th>
<th>OR$_{adj}$ (95% CI)</th>
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<tbody>
<tr>
<td>15-19 years</td>
<td>1.3 (1.01-1.71)</td>
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<tr>
<td>35-39 years</td>
<td>2.0 (1.48-2.82)</td>
</tr>
<tr>
<td>40-44 years</td>
<td>2.7 (1.90-3.74)</td>
</tr>
</tbody>
</table>

Mosher W. Contraception 2015; 92: 170-176

PERI-MENOPAUSE:
SPECIAL CONSIDERATIONS FOR CONTRACEPTION

• Contraception should be continued in sexually active women until:
  • Menopause – 1 year of amenorrhea, and/or FSH >40 (if using progestin-only methods)
  • In general, contraception can be discontinued by all women at the age of 55
• Many women experience perimenopausal menstrual dysfunction or vasomotor symptoms and hormonal contraceptive regimens can improve QOL in women with menstrual problems
• Usually advised that the lowest dose of estrogen that gives adequate cycle control for each individual woman should be used

Gebbie A. Menopause international 2010; 16(1): 33-37
Allen R. CMAJ 2013. 185(8): 565-573
RCOG: FSRH Clinical Guidance August 2017
CONTRACEPTIVE CHOICE OVER 40

• Choice Influenced by:
  • Frequency of intercourse, natural decline in fertility, sexual
dysfunction, menstrual dysfunction, desire for non-contraceptive
benefits, completion of childbearing
• Concurrent Medical Conditions:
  • Cardiovascular disease, diabetes, hypertension, hyperlipidemia,
obesity, breast cancer, gynaecological cancer
• Smoking >35 yrs

FSRH 2017

CHC USE IN PERIMENOPAUSE

• Advantages:
  • May help to maintain BMD
  • Improved cycle regularity, decreased menstrual flow &
pain
  • May reduce vasomotor symptoms
  • Protective effect against ovarian and endometrial
cancer

• Disadvantages
  • May be a small additional risk of breast cancer
  • Increased risk of VTE
  • May be small increased risk of ischaemic stroke (look
  for other risk factors)

Collaborative group on epidemiological studies on endometrial cancer. Lancet Oncol 2015; 16: 1061-70
Casper RF, Menopause 4:139 1997
CONTRACEPTION IN PERI-MENOPAUSE – WHEN TO STOP CHC?

Woman > 50 years old taking CHC who wishes to consider stopping contraception

Change to progestin-only pill (POP) or barriers
Wait at least 6 weeks
Check FSH on 2 occasions 6 weeks apart

If both FSH results are >30 U/L, use contraception for one more year then stop
If either FSH result < 30 U/L: Continue POP or barrier for 1 year
Re-test for FSH on 2 occasions 6 wks apart

FSRH, 2017
DMPA AND PERIMENOPAUSE

- No increased risk of VTE or MI
- No increased risk of breast cancer
- May improve vasomotor symptoms
- Decreased BMD during use due to relative hypoestrogenemia
  - Rapid decline in first year, then plateaus, then recovers after stopping
  - Postmenopausal women who have used DMPA, even up until menopause, do not have lower BMD compared to never users
- Annual review in women > 40 yrs, women >50 yrs should be counselled on alternate methods

Allen et al. CMAJ 2013. 185(7): 565-573
WHO Contraception. 1998;57(5):315-24
Mantha S. BMJ. 2012;345:e4944.

INTRAUTERINE CONTRACEPTION

- Advantage
  - Effective long acting reversible contraception (LARC)
  - Decreased menstrual bleeding (LNG-IUS)
  - Decreased risk of endometrial cancer (LNG-IUS and Cu-IUD)

- Disadvantage
  - Increase dysmenorrhea or menstrual flow (Cu-IUD)
  - Risk of expulsion, infection, perforation
  - If failure occurs, risk of ectopic pregnancy
LEVONORGESTREL RELEASING IUD

- If an LNG IUS (52mg, Mirena) is inserted after 45 years, it can be relied upon for contraception until the age of 55 years*
  - If amenorrheic, it should be removed after menopause
  - However, it cannot be relied upon for endometrial protection in the setting of HT

- LNG 52 mg is the only LNG IUD with indication for endometrial protection in the setting of Hormone Therapy

COPPER IUD

- Copper IUD with >300 mm² Copper that is inserted >40 yrs can remain until 1 year after LMP if a woman is >50 yrs
  - If a woman is under 50 yrs, the Copper IUD can remain until 2 years after LMP

- Women using IUD should have IUD removed once menopause is confirmed and/or contraception is no longer required
  - Case reports of actinomyocoses-like organisms, pyometria
SUMMARY

• CDC Medical Eligibility Criteria for Contraceptive Use App is AMAZING
• Women with migraines w/w/o aura should avoid CHC if additional risk factors present (cigarette smoking, HTN, obesity, history of cardiovascular disease, DVT, PE)
• Obese (BMI >30) who choose CHC should be counselled in extended cycle, and/or 4 day hormone free interval
• Risk of VTE in CHC users is overall low, but is highest in the first year
• CHC should not be avoided in women with mental health history, however healthcare providers should enquire about change in symptoms after CHC initiation
• Peri-menopausal women should be counselled on need for contraception, and should undergo yearly review due to health status changes
THANK YOU!

- Questions

Dr. Nicole Todd
drtoddmoa@gmail.com

Clinics:
- Pediatric and Adolescent Gynaeology Clinic, Hematology Gynaeology (Pediatric and Adult), Complex Contraception Clinic, UBC IUD Clinic

<table>
<thead>
<tr>
<th>Name</th>
<th>Mechanism</th>
<th>Dose/SA</th>
<th>Dimensions</th>
<th>Duration</th>
<th>Cost (CAD $)**</th>
<th>Effectiveness %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirena (Bayer)</td>
<td>Levonorgesterol 52mg</td>
<td>20 µg/day (but not measured at same time point or using the same calculation model as for Jaydess®)</td>
<td>Device: 32×32 mm Insertion Tube: 4.75 mm</td>
<td>5 years</td>
<td>350-400</td>
<td>&gt;99.</td>
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<td>Kyleena (Bayer)</td>
<td>Levonorgesterol 19.5 mg</td>
<td>14 µg/day (24 days after placement)</td>
<td>Device: 28x30 Insertion Tube: 2.80 mm</td>
<td>5 years</td>
<td>125</td>
<td>&gt;99</td>
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<td>Jaydess (Bayer)</td>
<td>Levonorgesterol 13.5mg Silver ring for ID</td>
<td>14 µg/day (24 days after placement)</td>
<td>Device: 28 x 30 Insertion Tube: 3.80 mm</td>
<td>3 years</td>
<td>125</td>
<td>&gt;99</td>
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<tr>
<td>Flexi T 300 (Trimedic)</td>
<td>Copper body</td>
<td>SA: 300 mm²</td>
<td>Device: 23mmx28mm Insertion Tube: 3mm</td>
<td>5 years</td>
<td>90</td>
<td>&gt;99</td>
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<td>Flexi T +300 (Trimedic)</td>
<td>Copper body</td>
<td>SA: 300 mm²</td>
<td>Device: 28mmx32mm Insertion Tube: 3mm</td>
<td>5 years</td>
<td>90</td>
<td>&gt;99</td>
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<tr>
<td><strong>Flexi T +380</strong></td>
<td>Copper body and arms</td>
<td>SA: 380 mm²</td>
<td>Device: 28mm x 32mm Insertion Tube: 3mm</td>
<td>5 years</td>
<td>90</td>
<td>&gt;99.</td>
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<td>(Trimedic)</td>
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<td><strong>Nova T (Bayer)</strong></td>
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<td>SA: 200 mm²</td>
<td>Device: 32mm x 32mm Insertion Tube: 32mm</td>
<td>2.5 years</td>
<td>180</td>
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<td>Copper body</td>
<td>SA: 300 mm²</td>
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<td>3 years</td>
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<td><strong>Mona Lisa 5</strong></td>
<td>Copper body and arms</td>
<td>SA: 380 mm²</td>
<td>Device: 31.8mm x 35.85mm Insertion Tube: 31.9mm</td>
<td>5 years</td>
<td>50-75</td>
<td>&gt;99.</td>
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<td><strong>Mona Lisa 10</strong></td>
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<td>SA: 380 mm²</td>
<td>Device: 31.85mm x 35.85mm Insertion Tube: 31.9mm</td>
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<td><strong>Liberte UT380</strong></td>
<td>Copper</td>
<td>SA: 380 mm²</td>
<td>Device: 36.4 mm x 32mm Insertion Tube: 32mm</td>
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<td><strong>Liberte UT380</strong></td>
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<td>SA: 380 mm²</td>
<td>Device: 34mm x 39.9mm Insertion Tube: 39.9mm</td>
<td>10 years</td>
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<td>Device: 32mm x 36mm Insertion Tube: 36mm</td>
<td>10 years</td>
<td>?</td>
<td>&gt;99.</td>
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THANK YOU!