Obesity and Contraception: What’s the Evidence?

Angeline Ti, MD MPH
Guest Researcher, Division of Reproductive Health
Centers for Disease Control and Prevention
Assistant Professor, Department of GYN/Ob
Emory University School of Medicine

National Title X Reproductive Health Conference
Kansas City
July 17, 2018
Disclosures

- Nothing to disclose

- The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Objectives

Describe the evidence for women with obesity and:

- safety of combined hormonal contraception
- effectiveness of hormonal contraception
- safety and effectiveness of emergency contraceptive pills

Describe the evidence for the association of hormonal contraceptive use and weight gain.
BACKGROUND
Why are we concerned about hormonal contraceptive use in women with obesity?

- Prevalence of obesity is increasing in the United States
- Increased risk of pregnancy complications
- Increased risk of health conditions that may affect safety of contraceptive use
  - CHCs and cardiovascular disease
- Obesity may affect drug metabolism
Outline: Obesity and Hormonal Contraception

- Obesity and contraceptive safety
  - CHCs and cardiovascular disease, especially venous thrombosis

- Obesity and contraceptive effectiveness
  - Pharmacokinetics
  - Pharmacodynamics
  - Pregnancy rates

- Hormonal contraception and weight gain

- Emergency contraceptive pills
  - Safety
  - Effectiveness
OBESITY AND CONTRACEPTIVE SAFETY
<table>
<thead>
<tr>
<th></th>
<th>CDC’s Contraceptive Guidance: US Medical Eligibility Criteria (MEC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No restriction for the use of the contraceptive method for a woman with that condition</td>
</tr>
<tr>
<td>2</td>
<td>Advantages of using the method generally outweigh the theoretical or proven risks</td>
</tr>
<tr>
<td>3</td>
<td>Theoretical or proven risks of the method usually outweigh the advantages – not usually recommended unless more appropriate methods are not available or acceptable</td>
</tr>
<tr>
<td>4</td>
<td>Unacceptable health risk if the contraceptive method is used by a woman with that condition</td>
</tr>
</tbody>
</table>
## US MEC: Obesity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cu-IUD</th>
<th>LNG-IUD</th>
<th>Implants</th>
<th>DMPA</th>
<th>POPs</th>
<th>CHCs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Obesity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Body mass index (BMI) ≥ 30 kg/m²</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>b. &lt; 18 years and BMI ≥ 30 kg/m²</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>History of bariatric surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Restrictive procedures</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>b. Malabsorptive procedures</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>COC:3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P/R: 1</td>
</tr>
</tbody>
</table>
Safety: Cardiovascular Disease

- **Obesity**: increased risk for cardiovascular events
  - Myocardial infarction (MI)
  - Stroke
  - Venous thromboembolism (VTE)

- **Combined hormonal contraceptive use**: increased risk for cardiovascular events
  - MI
  - Stroke
  - VTE

- **Theoretical concern** that combined effects of obesity and CHC use could further increase risk beyond individual effects
Safety: MI and Stroke

- Limited data: 2 studies

- RATIO Study, Netherlands: COC use and higher BMI
  - Increased risk for both MI and stroke

- Pooled analysis in US: COC use and higher BMI
  - No increased risk for both MI and stroke

- Non-standard BMI cut-offs

- If there is an increased relative risk, absolute risk likely remains low

Safety: VTE

- **Relative risk**
  - 5 studies find increased risk of VTE
    - COC use + obesity compared with no COC use + normal BMI
    - Limited data to assess risk at different BMI categories

- **Absolute risk**

<table>
<thead>
<tr>
<th>BMI</th>
<th>n</th>
<th>OR*</th>
<th>Absolute Risk of VTE (per 100,000 women)</th>
<th>Absolute Risk Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>194</td>
<td>0.8</td>
<td>27.0</td>
<td>N/A</td>
</tr>
<tr>
<td>20-24</td>
<td>681</td>
<td>1.0</td>
<td>33.7</td>
<td></td>
</tr>
<tr>
<td>25-29</td>
<td>216</td>
<td>1.4</td>
<td>47.2</td>
<td></td>
</tr>
<tr>
<td>30-34</td>
<td>77</td>
<td>1.8</td>
<td>60.7</td>
<td></td>
</tr>
<tr>
<td>35+</td>
<td>27</td>
<td>3.1</td>
<td>104.5</td>
<td>63-175</td>
</tr>
</tbody>
</table>

OBESITY AND CONTRACEPTIVE EFFECTIVENESS
Obesity and Contraceptive Effectiveness

- **Pharmacokinetics**
  - Drug levels in the body
  - Ethinyl estradiol, progestin levels

- **Pharmacodynamics**
  - Response to drugs at the site of action
  - Ovarian activity, ovulation, cervical mucus effects

- **Clinical outcomes**
  - Pregnancy
Combined oral contraceptives

- 14 studies that examine pregnancy rates
- 4 presented pregnancy rates by weight or BMI categories
  - None found pattern of increasing pregnancy rate with increasing weight or BMI
- 10 presented relative risks for pregnancy for higher vs lower weight or BMI

Relative risk of pregnancy by higher vs lower weight/BMI among COC users
Combined hormonal patch

- **Yamazaki, 2015**
  - Clinical trial (152 obese women, 1371 non-obese women)
  - Follow-up at least 6 cycles
  - aHR8.8 (95% CI 2.5-30.5) pregnancy for obese vs non-obese

- **Zieman, 2002**
  - Pooled analysis of 3 clinical trials (3,319 women)
  - 22,160 treatment cycles; 15 pregnancies
  - Association between baseline body weight and pregnancy ($p<.001$)
    - 5 pregnancies among women $\geq 90$ kg ($< 3\%$ of population)
  - No association between BMI and pregnancy rates

Obesity and Contraceptive Effectiveness

- **COCs**
  - Overall, pregnancy rates not different between obese and normal weight COC users
  - May be subgroups at higher risk—highest BMI or specific formulation
  - If there is an effect, most likely small, may not be clinically significant

- **Patch**
  - Two studies suggest that the patch may be less effective
  - Clinical significance unclear

- **Ring, Implants, POP, DMPA**
  - No pregnancy data
CONTRACEPTION AND WEIGHT GAIN
Contraception and weight gain

- Common concern among both patients and providers

- Proposed mechanisms:
  - Fluid retention
  - Increased fat deposition or muscle mass
  - Changes in satiety and appetite

- May impact initiation and continuation of users

- Additional consideration for obese patients who are trying to lose weight

Combined hormonal contraception

- Cochrane review of 49 randomized controlled trials: no clear evidence supporting causal association between CHCs and weight gain
  - 4 trials with placebo group: no association
  - 7 of 79 weight change comparison showed differences in weight change
  - Largest mean difference between groups was 1.8 kg (95% CI -0.73 to 4.33)

Progestin-only contraception

- 2009 systematic review of 9 studies:
  - Among adults, baseline weight or BMI not associated with weight gain
  - DMPA use may be associated with weight gain among overweight or obese adolescents

- Cochrane review of 22 studies (15 prospective and 7 retrospective): Limited evidence of weight gain with progestin-only methods
  - Actual amount of weight gain limited (<2kg for most studies)
  - POP and LNG-IUD: no difference in weight; some changes in body fat percentage
  - DMPA and implant: conflicting evidence; some increases when compared to no hormonal method

## US MEC: Obesity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cu-IUD</th>
<th>LNG-IUD</th>
<th>Implants</th>
<th>DMPA</th>
<th>POPs</th>
<th>CHCs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Obesity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Body mass index (BMI) ≥ 30 kg/m²</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2. &lt; 18 years and BMI ≥ 30 kg/m²</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>History of bariatric surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Restrictive procedures</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2. Malabsorptive procedures</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>COC:3 P/R: 1</td>
</tr>
</tbody>
</table>
Do you need to measure weight/BMI?

Prior to initiation:
- MEC: All methods are MEC category 1 or 2 for initiation
- SPR: Maybe helpful at baseline for monitoring changes

For follow-up:
- MEC: All methods are MEC category 1 or 2 for continuation
- SPR: Consider assessing for changes and counseling women who are concerned
OBESITY AND EMERGENCY CONTRACEPTIVE PILLS
<table>
<thead>
<tr>
<th>Condition</th>
<th>Cu-IUD</th>
<th>UPA</th>
<th>LNG</th>
<th>COC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity (BMI ≥ 30 kg/m²)</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>History of bariatric surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Restrictive procedures</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>b. Malabsorptive procedures</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
4 secondary analyses that pooled data from 6 clinical trials, combining various arms

- UPA and LNG: 2 RCTs (Glasier, 2011)
- UPA: 2 RCTs (Moreau, 2012)
- LNG: 2 RCTs (Kapp, 2015)
- LNG: 3 WHO trials (Gemzell-Danielsson, 2015)
**ECP effectiveness: UPA and LNG**

<table>
<thead>
<tr>
<th>BMI (kg/m$^2$)</th>
<th>Pregnancy Rate % [95% CI] Overall</th>
<th>UPA</th>
<th>LNG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal or underweight (&lt;25) n=2232</td>
<td>1.2 [0.8-1.8]</td>
<td>1.1 [0.6-1.9]</td>
<td>1.3 [0.8-2.2]</td>
</tr>
<tr>
<td>Overweight (25-29.9) n=744</td>
<td>1.7 [1.0-3.0]</td>
<td>1.1 [0.4-2.7]</td>
<td>2.5 [1.3-4.6]</td>
</tr>
<tr>
<td>Obese (≥ 30) n=469</td>
<td>4.3 [2.8-6.5]</td>
<td>2.6 [1.2-5.6]</td>
<td>5.8 [3.5-9.5]</td>
</tr>
</tbody>
</table>

**Odds Ratio [95% CI]**

<table>
<thead>
<tr>
<th>BMI (kg/m$^2$)</th>
<th>Odds Ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obese (≥ 30)</td>
<td>3.6 [1.96-6.53]</td>
</tr>
<tr>
<td>Normal or underweight (&lt;25)</td>
<td>Ref</td>
</tr>
</tbody>
</table>

## ECP effectiveness: UPA

<table>
<thead>
<tr>
<th>BMI (kg/m(^2)) Or Weight (kg)</th>
<th>Pregnancy rate % [95% CI]</th>
<th>Adjusted Odds Ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonobese (BMI &lt; 30) n=1830</td>
<td>1.6 [1.1-2.3]</td>
<td>Ref</td>
</tr>
<tr>
<td>Obese (BMI ≥ 30) n=351</td>
<td>3.1 [1.6-5.5]</td>
<td>2.1 [1.0-4.3] p=0.04</td>
</tr>
<tr>
<td>Weight ≤ 85 kg n=1883</td>
<td>1.6 [1.1-2.3]</td>
<td>Ref</td>
</tr>
<tr>
<td>Weight &gt; 85 kg n=298</td>
<td>3.4 [1.6-6.1]</td>
<td>2.2 [1.1-4.6] p=0.03</td>
</tr>
</tbody>
</table>

Moreau and Trussell *Contraception* 2012.
## ECP effectiveness: LNG

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Pregnancy rate % [95% CI] following LNG EC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 (n=249)</td>
<td>1.61 [0.44-4.06]</td>
</tr>
<tr>
<td>20-25 (n=873)</td>
<td>1.26 [0.63-2.24]</td>
</tr>
<tr>
<td>25-30 (n=367)</td>
<td>2.45 [1.12-4.60]</td>
</tr>
<tr>
<td>30-35 (n=149)</td>
<td>6.71 [3.26-11.99]</td>
</tr>
<tr>
<td>≥35 (n=93)</td>
<td>4.30 [1.18-10.64]</td>
</tr>
</tbody>
</table>

Kapp et al, *Contraception* 2015
ECP effectiveness: LNG

- 5812 women from 3 WHO trials on LNG ECP
- 56 pregnancies
- No correlation between increasing bodyweight or increasing BMI with pregnancy rate
ECP Effectiveness and Obesity

- 4 secondary analyses that pooled data from 6 clinical trials, combining various arms
  - UPA and LNG: increasing pregnancy rates with obesity; LNG may be ineffective with BMI > 30
  - UPA: increasing pregnancy rates with obesity
  - LNG: 2 studies with conflicting evidence
    - Increasing pregnancy rates with obesity; LNG may be ineffective with BMI > 30
    - No effect of increasing BMI or body weight on pregnancy rate

Safety

- Data on adverse events of ECPs limited; further limited in obese women
- Adverse events did not include complications or comorbidities of obesity, e.g., thrombosis or CVD events
- Little theoretical concern about adverse events, including for women with obesity

US MEC: Emergency Contraception

- Copper IUD most effective method of emergency contraception, regardless of weight
- Possible decreased effectiveness of ECPs among women with obesity
- No safety concerns for ECP use among women with obesity
Conclusions

- The current evidence and guidance suggest that all forms of contraception, including emergency contraception, are generally safe and effective for obese adolescents and women.
- Additional considerations for estrogen, adolescents and DMPA, the contraceptive patch, and ECPs.
- Evidence around weight gain varies by method:
  - Objective monitoring can assist in counseling.
2016 U.S. MEC and SPR App

MEC by Condition

MEC by Method

SPR

Select Method (MEC)
- Intrauterine Contraception
- Progestin-only Contraceptives
- Combined Hormonal Contraceptives
- Barrier Methods
- Fertility Awareness-based Methods
- Lactational Amenorrhea Method
- Coitus Interruptus

SPR
- How To Be Reasonably Certain That A Woman Is Not Pregnant
- Cu-IUD
- LNG-IUD
- Implants
- Injectables
- Combined Hormonal Contraceptives
- Progestin Only Pills
Tools and Aids

- Online access to full guidelines
- MEC summary table in English, Spanish
- SPR quick reference charts
- MEC Wheel
- Continuing Education Activities
- Speaker-ready slides
- Contraceptive Effectiveness Charts
- Online alerts to receive updates
- eBook for SPR
Resources

- CDC evidence-based family planning guidance:
  http://www.cdc.gov/reproductivehealth/unintendedpregnancy/USMEC.htm
  http://www.cdc.gov/reproductivehealth/unintendedpregnancy/USSPR.htm

- Sign up to receive alerts!

- Further reading and acknowledgements