U.S. Medical Eligibility Criteria for Contraceptive Use, 2010

Adapted from the World Health Organization Medical Eligibility Criteria for Contraceptive Use, 4th edition
U.S. Selected Practice Recommendations for Contraceptive Use, 2013
Adapted from the World Health Organization Selected Practice Recommendations for Contraceptive Use, 2nd Edition
**Contraceptives: The “New Paradigm”**

- **Combined Hormonal Contraceptives (CHC)**
  - OCs, Patch, Ring

- **Continuous Progestin Contraceptives**
  - Progestin-only Pill (POP)
  - Injectable (DMPA)
  - Implant (ENG contraceptive implant)

- **Intrauterine Contraception**
  - Copper T-380A, LNG-IUS

- **Barrier Methods**

- **Natural Family Planning**
Figure 3-1 Comparing typical effectiveness of contraceptive methods

More effective

Less than 1 pregnancy per 100 women in one year

- Implant
- Vasectomy
- Female Sterilization
- IUC

How to make your method most effective

- After procedure, little or nothing to do or remember
- **Vasectomy**: Use another method for first 3 months

- **Injectable**: Get repeat injections on time
- **Pills**: Take a pill each day
- **Patch, ring**: Keep in place, change on time
- **Diaphragm**: Use correctly every time you have sex

Less effective

18 or more pregnancies per 100 women in one year

- Male Condom
- Female Condom
- Sponge
- Withdrawal
- Spermicides
- Fertility Awareness-Based Methods

Source: Adapted from WHO 2007

**Fertility awareness-based methods**: Abstain or use condoms on fertile days. Newest methods (Standard Days Method and TwoDay Method) may be the easiest to use and consequently more effective.
Why LARC* Methods?
*Long Acting Reversible Contraception

- IUCs and Implants are “forgettable”
  - Single motivational act for insertion
  - Do not require episodic, daily, weekly, monthly, or every 12 week user initiative
  - No need to take time to refill prescriptions or risk that prescriptions will not be refilled on time
  - Give continuous 24/7/365 contraceptive protection
  - Provide long term protection...3-10 years
Why LARC* Methods?

*Long Acting Reversible Contraception

- Are the most effective reversible methods available
- Are among the safest contraceptive methods...very few U.S.-MEC category 3 or 4 grades
- Have superior continuation rates and highest patient satisfaction among methods
- Are an alternative to surgical sterilization
- Are the most cost effective and cost saving methods
Implant

- Brand name: Nexplanon
- Contains etonogestrel
- Effective for 3 years

(Etonogestrel) ENG Implant: Nexplanon

- Progestin only, implant effective for up to 3 years
- Studied in 17 countries, including US
  - Marketed in 30 countries; >2.5 million insertions
- Inserted subdermally between biceps and triceps
- Must be inserted and removed only by clinicians that have completed training program
ENG Implant: Mechanism of Action

- Inhibits ovulation – none
  - For 30 months
- Increases viscosity of cervical mucus
- Initial study (Glasier A, *Contraception* 2002)
  - No pregnancies reported in 73,429 cycles
- US studies (Implanon package insert)
  - 6 pregnancies reported in 20,648 cycles
  - Each conception immediate after removal
ENG Implant: Candidates

- Women who want continuous pregnancy protection with long duration of action (2-3 years)
- Accepting of unpredictable vaginal bleeding patterns
- Precautions (Implanon package insert)
  - Known or suspected pregnancy
  - Current or past history of thrombotic disease
  - Hepatic tumor, active liver disease
  - Known or suspected breast cancer
  - Hypersensitivity to any component of Implanon
  - Less than 6 weeks post partum
ENG Implant: Vaginal Bleeding

- Smaller *amount* of bleeding than cycling women
- *Number* of bleeding days in implant users is similar to natural cycles, but the pattern is unpredictable
  - Patients with a favorable bleeding pattern in the first 90 days tend to have a favorable pattern
  - More than 1/2 with an unfavorable pattern initially will have an improved pattern over time
- Continuous progestin *prevents* EM hyperplasia; endometrial biopsy unnecessary for this purpose
ENG Implant: Vaginal Bleeding

• Counseling points
  – You will have fewer bleeding episodes
  – You will have the same or fewer bleeding days

• But,
  – Your bleeding days, episodes will be unpredictable
  – You may have more spotting days than before
Levonorgestrel Intrauterine System (LNG IUS)

- Brand name: Mirena®
- 20 mcg levonorgestrel/day
- Approved for 5 years’ use
- Amenorrhea in ~20% of users by 1 year

Copper-T IUD

- Brand name: Paragard®
- Copper ions
- Approved for 10 years’ use
- Can be used as emergency contraceptive

Characteristics of Intrauterine Contraception

- Highest patient satisfaction among methods
- Rapid return of fertility
- Safe
- Immediately effective
- Long-term protection
- Highly effective

## Intrauterine Contraception in the U.S.

<table>
<thead>
<tr>
<th></th>
<th>ParaGard®</th>
<th>Mirena®</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>Copper ions</td>
<td>Levonorgestrel</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>10 years</td>
<td>5 years</td>
</tr>
<tr>
<td><strong>Efficacy (typ)</strong></td>
<td>0.8 failures/hwy</td>
<td>0.1 failures/hwy</td>
</tr>
<tr>
<td><strong>Benefit</strong></td>
<td>No hormones</td>
<td>Less bleeding</td>
</tr>
<tr>
<td><strong>Non contraceptive uses</strong></td>
<td>None</td>
<td>Menorrhagia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Endometriosis</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>Less expensive</td>
<td>More expensive</td>
</tr>
</tbody>
</table>
IUC: Use in Nulliparous Women

- Use of IUCs by nulliparous women with low risk of PID is safe and effective\(^1-^4\)
- LNG-IUS is appropriate for nulliparous women with menorrhagia and/or dysmenorrhea
- IUC expulsion, bleeding, and pain are slightly more likely among nulliparous women\(^2-^5\)

Pre-IUC Insertion Screening

- Evidence supports no routine screening tests
  - Ct, GC: if high risk sexual behaviors or <26 yo and annual screening Ct has not been done
  - Pregnancy test: only if pregnancy suspected
  - Pap smear: only if due for a routine Pap
  - Hematocrit: only if anemia suspected

- Any indicated screening test can be done on the day of IUC insertion
### The Contraceptive CHOICE Project

<table>
<thead>
<tr>
<th>Method</th>
<th>n</th>
<th>1 year continuation</th>
<th>% Very satisfied</th>
<th>% Not satisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td>LNG-IUS</td>
<td>1,890</td>
<td>88</td>
<td>70</td>
<td>14</td>
</tr>
<tr>
<td>Cu- IUD</td>
<td>434</td>
<td>84</td>
<td>66</td>
<td>20</td>
</tr>
<tr>
<td>Implant</td>
<td>522</td>
<td>83</td>
<td>55</td>
<td>21</td>
</tr>
<tr>
<td>DMPA</td>
<td>313</td>
<td>56</td>
<td>42</td>
<td>46</td>
</tr>
<tr>
<td>OCPs</td>
<td>478</td>
<td>55</td>
<td>41</td>
<td>46</td>
</tr>
<tr>
<td>Patch</td>
<td>99</td>
<td>49</td>
<td>35</td>
<td>56</td>
</tr>
<tr>
<td>Ring</td>
<td>431</td>
<td>54</td>
<td>47</td>
<td>47</td>
</tr>
<tr>
<td>LARC</td>
<td>2,846</td>
<td>86</td>
<td>67</td>
<td>16</td>
</tr>
<tr>
<td>Non-LARC</td>
<td>1,321</td>
<td>55</td>
<td>43</td>
<td>47</td>
</tr>
</tbody>
</table>

Combined Hormonal Contraceptives

- All four methods have similar...
  - Contraceptive efficacy
  - Menstrual bleeding patterns
  - Side effects
  - Complications
  - Monthly cost

- Major difference: delivery system
## OC Cycle Variations

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quick start</td>
<td>Allows immediate method initiation any time in cycle</td>
</tr>
<tr>
<td>Shortened HFI (24 d on/4 d HFI)</td>
<td>More forgiving of late OC cycle start (probably improving efficacy)</td>
</tr>
<tr>
<td>Extended cycle</td>
<td>Fewer menstrual events and symptoms</td>
</tr>
<tr>
<td>• 84 d on /7 HFI</td>
<td>Menses 4 time per year</td>
</tr>
<tr>
<td>• 84 d on/ 7 E only</td>
<td></td>
</tr>
<tr>
<td>• 365 days on</td>
<td>No menstrual periods for 1 year</td>
</tr>
</tbody>
</table>

**HFI:** hormone free interval
Quick Start: Rationale

- When prescribed in advance, why do some women fail to start OCs with the next menses?
  - Intervening pregnancy
  - Change in motivation to use OCs
  - Confusion regarding when to start OCs
  - Effort necessary to receive OCs from pharmacy
  - Fear of side effects

- What if....
  - OCs routinely could be started at the moment that they are prescribed?
Quick Start (QS) Compared to Conventional Start (CS)

- 1,716 women <25 yo; 3 public family planning clinics
- Randomly assigned to QS or CS
- Follow up interviews at 3 and 6 months
- Findings
  - QS users more likely to use 2nd pack (OR=1.5), but continuation rates same at 3, 6 months
  - QS group 10% less likely to become pregnant
  - 81% rated QS as acceptable or preferable to waiting
  - Serious adverse events low, same in both groups

Quick Start: Advice to Patients

Assume 28 day cycle

EC: emergency contraception

If unprotected sex d 7-14 & EC, pregnancy is possible
Use EC if unprotected sex (can be used up to 5 days later)
Use condoms for next 7 days

No back up needed

OC start day

1 6 14 21 24 28

Preg test
Extended CHC: Why Bother?

HFI = Hormone Free Intervals

- Fewer HFIs (extended CHC regimen)
  - Fewer bleeding episodes
  - Fewer menstrual symptom episodes
  - Possibly less severe symptoms with menses
- Shorter HFIs
  - Fewer symptomatic days per menses
  - Greater tolerance of missed late method initiation
- Shifting of HFI (menstrual regulation)
  - Episodic delay in onset of menses for convenience
Clinical Uses: Extended CHC Regimens

- Convenience
  - Preference for long term oligomenorrhea
  - Episodic delay in onset of menses
  - More consistent schedule of OC use

- Minimize bleeding episodes
  - Idiopathic menorrhagia or 2º to fibroids, anatomic conditions
  - Clotting deficiencies: ITP, Von Willebrand disease, aplastic anemia
Clinical Uses: Extended CHC Regimens

- Minimize menstrual pain
  - Endometriosis and adenomyosis
  - Chronic pelvic pain
  - Recurrent functional ovarian cysts
  - Primary or secondary dysmenorrhea

- Minimize systemic effects of menses
  - PMS and PMDD manifestations
  - Menstrual migraine or other headaches
  - Menstrual seizures
Clinical Uses: Extended CHC Regimens

- **Menstrual regulation**
  - Vacation, exams, athletic events
- **Shortened HFI**
  - Pre-menstrual or menstrual symptoms: bloating, breast tenderness, mood swings
  - Monthly menstrual migraine or other headaches; menstrual seizures
  - Primary or secondary dysmenorrhea
Summary of 5 Extended OC Studies

- Continuous OC users have:
  - Fewer scheduled bleeding days/year
  - Fewer scheduled bleeding episodes/year
  - Shorter withdrawal bleeds

- (Unscheduled) spotting rates similar in both groups

- Amenorrhea increasingly common with longer use

- Successful use of extended regimens up to 12 months

- 2/3 of women who try extended regimens achieve long term use
Extended OC Regimens

- **Seasonale ®** 84 days on/ 7 day HFI
- **Seasonique ®** 84 days on/ 7 day estrogen
- **Lybrel®** 365 days of active OCs
- “Fixed” extended monophasic OCs
  - “Bi-cycling” 42 days (6 weeks)
  - “Tri-cycling” 63 days (9 weeks)
  - “Quad cycling” 84 days (12 weeks)
  - Then a 3-7 day HFI
Extended CHC Regimens

- **Ortho EVRA patch**
  - Apply patch for 7 days; replace on “patch day”
  - Fixed regimen: 6, 9, 12 weeks (or more), then HFI
  - Variable regimen: use till bleeding, then 3-7d HFI

- **Nuva Ring**
  - Use ring for 3-4 weeks, then insert new ring
  - Fixed regimen: 2, 3, or 4 rings, then HFI
  - Variable regimen: use till bleeding, then 3-7d HFI

- **Limited data on these MOC as extended CHC**
Patient Counseling Issues

- Why 84 days and not longer?
- Is it a problem not to have a period for 3 months?
- Will I bleed more when my period does occur?
- Is there a risk in taking additional OCs over time?
- What if I’m already using cyclic OCs?
- Can I use my tricyclic OC to do this?
- Is there anyone who shouldn’t use this regimen?
The Message: Extended CHC

- High quality studies show that extended OC regimens can be used for as long as one year.
- Extended OC regimens can be used with Seasonale® or conventional monophasic OCs.
- 2/3 of those who tried extended OCs continued use.
- The Patch and Ring can be used in an extended regimen, but there is little data regarding this use.
- Extended CHC regimens can be offered to all women or only those with specific indications.
Why The Trend Toward a 4-Day Hormone-Free Interval (HFI)?

- No head-to-head studies of 24/4 regimens compared to 21/7 regimens
- What we want to know...
  - Is a 24/4 regimen really more effective than 21/7?
  - Are bleeding patterns different between the two?
  - Are there fewer menstrual symptoms with a 4 day HFI compared to a 7 day HFI?
  - How much of the difference is marketing vs. real advantages?
4-Day Hormone-Free Interval (HFI) 
What We Do Know

- Lower hormone doses are cleared more rapidly than with older (and higher dose) OCs
- Higher FSH levels with 7 day HFI than 4 day HFI
- More follicle growth with 7 day HFI than 4 day HFI
- 24/4 cycles (compared to 21/7) theoretically will ...
  - Be more forgiving of late OC initiation
  - Will have marginally lower failure rates
24/4 OC Products

- **YAZ®** (Bayer [Berlex]): 4/06
  - EE 20 mcg + drospirenone 3 mg
  - 24 days active, 4 days hormone free
  
  *Vs. Yasmin*
  - EE 30 mcg / drospirenone 3 mg
  - 21 days active, 7 days hormone free

- **Loestrin 24®** (Warner Chilcott): 2/06
  - EE 20 mcg + nor acetate 1 mg + Fe fumarate
  - 24 days active, then 4 days Fe only
  
  *Vs. Loestrin 1/20*: EE 20 mcg + nor acetate 1 mg
  - 21 days active, 7 days hormone free
Emergency Contraception

Plan B available over-the-counter! No age restriction!

- over-the-counter cost = around $40-50

- Family Planning—$0-$43 based on sliding fee scale

- Can be taken up to 5 days after unprotected sex

- Will only prevent pregnancy—will not stop a pregnancy if fertilization and implantation has already occurred.

- A partner or parent can buy EC.
Ulipristal Acetate (UPA): Ella®

- Selective progesterone receptor modulator
- Taken orally in single 30 mg dose
- Approved in Europe(2009) for up to 5 days
- Mechanism of action
  - Prevent ovulation, with follicles up to 18-20 mm
  - Inhibits implantation, but higher dose required
- Failure rate vs. LNG (meta-analysis 0-120 hr)
  - UPA 1.3% vs. LNG 2.2%
  - Odds Ratio = 0.55 (0.32-0.93)
Ulipristal Acetate (UPA): Ella®
Glasier AF, Lancet 2010;375:555

- Comparative trial of UPA 30 mg vs LNG 1.5 mg
  - 1,696 women used with 72 hours of intercourse
    » Failure rates: UPA 1.8% vs. LNG 2.6% (OR=0.68)
  - 203 women used with 72-120 hrs of intercourse
    » Failures: UPA- none vs. LNG- 3 pregnancies
  - Headache: UPA=19%, LNG=19%

- Conclusion
  - UPA is “not inferior” to LNG
  - UPA is effective for up to 5 days after exposure
NuvaRing Duration of Action

- Designed to be used 21 days on/7 days off
  - Advise initiation on or before day 5 (+ back up 7 days) for new start users
- Duration of action is at least 4 weeks, possibly longer
- Once removed, earliest ovulation is in 13 days
- Alternative use regimens
  - “Package insert”: 21 on/7 days off
  - 4 weeks on, then 4-7 day hormone free interval
  - “Calendar month”: use 1-25th, then off till the 1st
Ovulation Inhibition With NuvaRing®

- NuvaRing® effectively inhibits ovulation
  - During recommended use
  - During extended use (at least up to 4 weeks)
  - After early removal (3 days use will delay ovulation)
  - After late insertion (up to 13mm follicle)

- There is a rapid return to ovulation after removing NuvaRing®

Mulders & Dieben, Fertil Steril 2001; 75:665-70
Mulders et al. Human Reprod 2002;17:2594-9
Extended Regimen Nuva Ring

- 429 women randomized, 289 (67%) completed
- Compared 4 regimens (21 days/ring; 7 day HFI)
  - 28 day, 49 day, 91 day, 364 day cycles
- All schedules well tolerated, completion rate higher for shorter cycles
- With longer regimens
  - Scheduled bleeding days less
  - Spotting days increased (least with 28 day cycle)
- Adverse events, BP, weight, lab findings comparable

Miller, Obstet Gynecol 2005;106:473
OrthoEvra: Labeling Change 11/05

- Basis for labeling change: studies showing
  - Average ethinyl estradiol (EE) concentration **60% higher** than 35 mcg OC
  - Peak of EE is **25% lower** than 35 mcg OC
  - Cumulative increase in EE levels over 3 weeks
  - "Not known" whether there are changes in the risk of serious adverse events

- Persistent *unsubstantiated* "reports" of higher rates of venous (?) arterial) events
OrthoEVRA and CV Events

- New Ortho advisory issued 2/16/2006
  - BCDSP: no increased risk of stroke or MI vs. OC
  - i3 Drug Safety
    » No increased risk of stroke or MI vs. OC
    » 2-fold increase in VTE in Evra vs. OC users
- Clinical significance… until more is known
  - Higher level of caution regarding patch use in women with venous or arterial risk factors
  - Avoid extended patch regimens (>3 in a row)
  - Use same precautions for patch that apply to OCs
Injectable

- Depot Medroxyprogesterone Acetate (DMPA)
- Brand name: Depo-Provera®
- Intramuscular or subcutaneous injection every 3 months

DMPA and Osteoporosis

What we know

- In most studies, women who used DMPA had 5-10% lower bone mineral density than non-hormone users
- Effect is seen in adolescents as well as older women
- No relationship of duration of use and BMD loss
- In populations of women tested, bone loss is reversible when DMPA stopped

But…

- There are no studies of fracture risk in DMPA users
- BMD is not an established surrogate marker for fracture risk in younger women
U.S. MEC, 2010: DMPA, Age, and BMD

❖ Menarche-18 years old
  – 2: limited evidence shows decreased BMD over time; no studies evaluate impact on peak BMD

❖ 18-45 years old
  – 1: current DMPA users had decreased BMD, usually within 1 SD of normal values

❖ Older than 45 years old
  – 2: in PM women, no difference in BMD between former DMPA users and never users
What Is the Issue? Fracture Risk!!

Women under 40 years old

- Low impact fractures due to osteoporosis *very* rare
- No data that DMPA use increases fracture risk before menopause, but it is extremely unlikely
- No data that DMPA increases post-menopausal fractures in prior users who stopped < 40 years old
- Impact on an individual’s “peak BMD” is unknown

However

- If DMPA reduces BMD, many years left to regain it
- No reason to time limit or offer “drug vacation”
## Body Weight and Contraception

<table>
<thead>
<tr>
<th>Weight Gain</th>
<th>OC</th>
<th>Patch</th>
<th>DMPA</th>
<th>Implant</th>
<th>IUC</th>
<th>Tubal</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes*</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Increased failure rate in obese women</td>
<td>No Δ</td>
<td>Yes #</td>
<td>No Δ</td>
<td>No Δ</td>
<td>No Δ</td>
<td>No Δ</td>
</tr>
<tr>
<td>Medical risk in obese women</td>
<td>DVT</td>
<td>No studies</td>
<td>None</td>
<td>None</td>
<td>Difficult insertion</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>WHO-MEC</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>Not rated</td>
</tr>
</tbody>
</table>

*Mainly in obese adolescents and those who experience a ≥ 5% body weight increase within 6 months of DMPA initiation

# In women who weigh ≥ 90 kg, increase of 2-4 failures/100 couples/year
Hormonal Contraception Plus Other Drugs: What Does the Evidence Say?

In hormonal contraceptive (HC) users taking other drugs:

- There are a few case reports of pregnancies
- Many studies evaluate the effect of a challenge drug on hormone levels and breakthrough bleeding
  - Most of these with OC users
- Very few studies of drug effects on ovulation
- Virtually no studies of pregnancy rates...why?
  - Pregnancy is a rare event
  - RCTs are difficult; observational studies open to bias
  - Little incentive to fund these trials
**Urban Legend**
- In women using hormonal contraceptives, the addition of a (non enzyme-inducing) antibiotic will increase BTB, ovulation, and pregnancy risk

**The Reality**
- There is no evidence that antibiotics will...
  - Reduce E+P in a clinically significant way
  - Increase pregnancy rates
Antibiotics in OC Users

Based upon good quality studies, these antibiotics do not decrease steroid levels in women using OCs

- Ampicillin, amoxicillin
- Clarithromycin
- Metronidazole
- Quinolone antibiotics (ciprofloxacin, ofloxacin)
- Doxycycline, tetracycline
- Fluconazole
Recommendations: Antibiotic Use in Hormonal Contraceptive Users

- In HC users taking a short or long course of antibiotics, there is no evidence-based reason to routinely recommend
  - Back-up contraception
  - A change to a more effective method

- If a women is informed of a potential interaction, the extremely low magnitude of risk must be stressed

- Pregnancies that occur in women using both HC and antibiotics are due to other factors
10 (+1) practical, evidence-based recommendations for you to improve contraceptive care now
10 (+1) Recommendations To Improve Contraceptive Care Now

1. Pelvic exam? It isn’t mandatory
   - Do not require pelvic examination before you prescribe an oral contraceptive.

2. Provide more, not less
   - Prescribe (when possible, dispense) 6 to 12 months of an OC at office visits

3. Make the case for long-acting reversibles
   - Use intrauterine devices and subdermal implants as first-line contraception more often

_OBG Management · 2011; 23 (8): 25-29_
4. Take advantage of broader benefits
   – Use hormonal contraceptives for non-contraceptive indications

5. To encourage continuation, begin now
   – Get a “quick start” to improve adherence to oral contraceptives

6. Move away from every-day regimens
   – Consider a nondaily combined method, such as the patch or the vaginal ring, for current OC users

*OBG Management* · 2011; 23 (8): 25-29
10 (+1) Recommendations To Improve Contraceptive Care Now

7. Preemptive prescribing
   – Prescribe EC before your patient needs it

8. Get to know Ella
   – Become familiar with ulipristal acetate (Ella) for EC

9. Pursue two urogenital pathogens
   – When you are not performing a speculum examination, screen for *N. gonorrhoeae* and *C. trachomatis* with a vaginal swab specimen or urine-based specimen

*OBG Management* · 2011; 23 (8): 25-29
10 (+1) Recommendations To Improve Contraceptive Care *Now*

10. **Now not later: An IUD, post-evacuation**
   - Consider immediate, rather than delayed, IUD insertion after uterine evacuation for spontaneous or elective abortion in women who desire this form of contraception

11. **Offer office-based hysteroscopic sterilization**

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