# New methods added to the MEC, 5th Edition

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WHO/ SRH/ CFC

World Health Organization

human reproduction programme hrp

research for impact

UNDP-UNFPA-UNICEF-WHO-THE WORLD BANK

# Methods of contraception included in MEC, 4th Edition

- Combined oral contraceptives
- Combined hormonal contraceptives (1 month injectables, patch, vaginal ring)
- Progestogen-only contraceptives (pills, implants, 2-3 month injectables)
- Emergency contraceptive pills
- IUDs (copper bearing and levonorgestrel)
- Emergency IUD
- Barrier methods (condoms, spermicides & diaphragm)
- Fertility awareness-based methods
- Lactational amenorrhoea (LAM)
- Coitus Interruptus
- Sterilization (male and female)

# New methods added to MEC 5th edition

- Subcutaneously-administered depot medroxyprogesterone acetate(DMPA-SC)
- Sino implant (II)
- Ulipristal acetate (UPA)
- Progesterone-releasing vaginal ring (PVR)

# SUBCUTANEOUSLY - ADMINISTERED DEPOT MEDROXYPROGESTERONE ACETATE (DMPA-SC)

# DMPA-SC

- Depot medroxyprogesterone acetate delivered subcutaneously (DMPA SC) at dose of 104 mg/0.65 mL

- Important service delivery implications:

  - Self-administration feasible and acceptable to both adolescents and adults

# DMPA-SC: Summary of Evidence

- **Obesity (8 studies)**
  - Contraceptive efficacy, weight change and other adverse events similar across BMI groups
- **Age (3 studies)**
  - Declines in BMD, no differences in weight change or bleeding patterns by age group
- **Endometriosis (2 studies)**
  - Declines in BMD, few serious adverse events
- **HIV (1 study)**
  - No difference in serious adverse events (SC vs. IM)

- Among **healthy women (3 studies)**, evidence suggests DMPA-SC may be similar to DMPA-IM

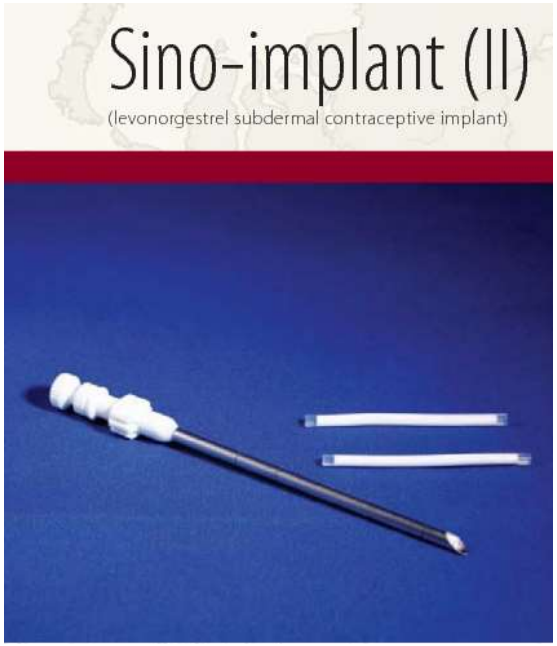
# DMPA-SC

- No change in existing MEC recommendations for DMPA warranted with inclusion of DMPA-SC as a new method.

# SINO-IMPLANT (II)

# Background: Sino-implant (II)

- 2-rod, 150 mg LNG implant manufactured in China
- Currently used by millions of women worldwide (mostly Indonesia & China)



# SI (II) Efficacy

- Systematic review of RCTs with > 15000 users found:
  - Year 1 pregnancy rates ranged from 0-0.1%
  - Cumulative pregnancy rates through year 4 from 0.9-1.06%
- Post-marketing surveillance in Madagascar, Kenya and Pakistan indicates high efficacy and satisfaction with method

Source: Steiner MJ et al. Sino-implant (II)--a levonorgestrel-releasing two-rod implant: systematic review of the randomized controlled trials. Contraception. 2010;81(3):197-201.

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# ULIPRISTAL ACETATE

# Ulipristal Acetate (UPA)

- Selective progesterone receptor modulator
- Single dose 30mg effective up to 120 hours
- Delays ovulation
- Approved in EU in 2009, US in 2010
- Currently registered in 72 countries

# MEC, 4th Edition ECP Recommendations

## EMERGENCY CONTRACEPTIVE PILLS (ECPs)
## (including levonorgestrel contraceptive pills and combined oral contraceptive pills)

ECPs do not protect against STI/HIV. If there is risk of STI/HIV (including during pregnancy or postpartum), the correct and consistent use of condoms is recommended, either alone or with another contraceptive method. Male latex condoms are proven to protect against STI/HIV.

| CONDITION<br>* additional comments at end of table | CATEGORY | CLARIFICATIONS/EVIDENCE |
|---|---|---|
| PREGNANCY | NA | NA = not applicable<br>**Clarification**: Although this method is not indicated for a woman with a known or suspected pregnancy, there is no known harm to the woman, the course of her pregnancy, or the fetus if ECPs are accidentally used. |
| BREASTFEEDING | 1 | |
| PAST ECTOPIC PREGNANCY | 1 | |
| HISTORY OF SEVERE CARDIOVASCULAR COMPLICATIONS*<br>(ischaemic heart disease, cerebrovascular attack, or other thromboembolic conditions) | 2 | |
| ANGINA PECTORIS* | 2 | |
| MIGRAINE* | 2 | |
| SEVERE LIVER DISEASE*<br>(including jaundice) | 2 | |
| REPEATED ECP USE | 1 | **Clarification**: Recu<br>requires further coun<br>repeated ECP use m<br>as 2, 3 or 4 for CHC |
| RAPE* | 1 | |

### ADDITIONAL COMMENTS

**HISTORY OF SEVERE CARDIOVASCULAR COMPLICATIONS**
The duration of use of ECPs is less than that of regular use of COCs or POPs and thus would be expected to have less clinical impact.

**ANGINA PECTORIS**
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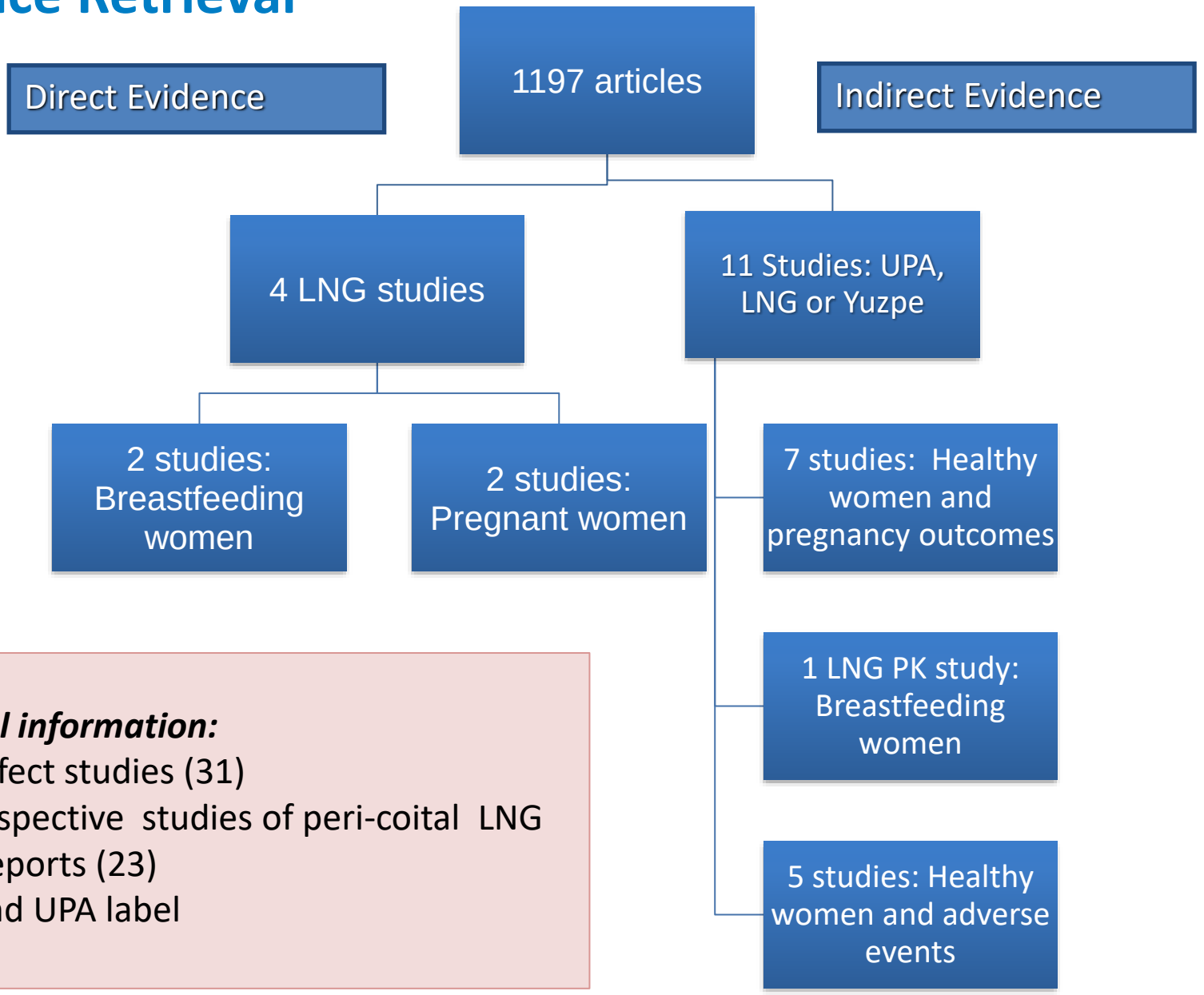
**MIGRAINE**
The duration of use of ECPs is less than that of regular use of COCs or POPs and thus would be expected to have less clinical impact.

**SEVERE LIVER DISEASE (INCLUDING JAUNDICE)**
The duration of use of ECPs is less than that of regular use of COCs or POPs and thus would be expected to have less clinical impact.

**RAPE**
There are no restrictions for the use of ECPs in cases of rape.

# Evidence Retrieval




***Additional information:***

- Side effect studies (31)
- Six prospective studies of peri-coital LNG
- Case reports (23)
- LNG and UPA label

# NEW ECP Recommendations

| Condition | COC | LNG | UPA |
|---|---|---|---|
| Pregnancy | NA | NA | NA |
| Breastfeeding | 1 | 1 | 2 |
| Past ectopic pregnancy | 1 | 1 | 1 |
| Obesity | 1 | 1 | 1 |
| History of severe cardiovascular disease | 2 | 2 | 2 |
| Migraine | 2 | 2 | 2 |
| Severe liver disease (including jaundice) | 2 | 2 | 2 |
| CYP3A4 inducers | 1 | 1 | 1 |
| Repeated emergency contraceptive pill use | 1 | 1 | 1 |
| Rape | 1 | 1 | 1 |

COC= combined oral contraceptives; LNG = levonorgestrel; UPA = ulipristal acetate;
NA = not applicable

# ECPs and Breastfeeding

| Condition | COC | LNG | UPA |
|---|---|---|---|
| **Breastfeeding** | **1** | **1** | **2** |

**Clarification**: Breastfeeding is not recommended for 1 week after taking UPA since it is excreted in breast-milk. Breast-milk should be expressed and discarded during that time.

# ECPs and Obesity

| Condition | COC | LNG | UPA |
|---|---|---|---|
| **Obesity** | **1** | **1** | **1** |

**Clarification:** ECPs may be less effective among women with BMI ≥ 30 kg/m$^2$ than among women with BMI < 25 kg/m$^2$. Despite this, there are no safety concerns.

**Evidence:** There is limited evidence from one study that suggests obese women with BMI ≥ 30 kg/m$^2$ experience an increased risk of pregnancy after use of LNG compared with women with BMI < 25 kg/m$^2$. Two studies suggest obese women may also experience an increased risk of pregnancy after use of UPA compared with non-obese women, though this increase was not significant in one study.

# ECPs and CYP3A4 INDUCERS

| Condition | COC | LNG | UPA |
|---|---|---|---|
| **CYP3A4 INDUCERS** (E.g. rifampicin, phenytoin, phenobarbital, carbamazepine, efavirenz, fosphenytoin, nevirapine, oxcarbazepine, primidone, rifabutin, st john's wort/hypericum perforatum) | **1** | **1** | **1** |

**Clarification:** Strong CYP3A4 inducers may reduce the effectiveness of ECPs.

**Evidence:** According to labelling information, rifampicin markedly decreases UPA levels by 90% or more which may decrease its efficacy. Theoretical concerns therefore extend to use of other CYP3A4 inducers as well as to COC and LNG ECPs, which have similar metabolic pathways to UPA. A small pharmacokinetic study found that concomitant efavirenz use decreased LNG levels in women taking LNG ECP (0.75 mg) by 56% compared with LNG ECP alone.

# PROGESTERONE-RELEASING VAGINAL RING (PVR)

# Progesterone- Releasing Vaginal Ring (PVR)

- Matrix design
- Diameter 58 mm/ Cross-section 8.4 mm
- Delivers 10mg/day over 3 months
- Serum levels of 10-20 nmol/L [~7ng/ml]
- Specifically designed for breastfeeding

- Registered in 9 Latin American countries - Acceptability studies underway in Africa

# NEW Recommendations for PVR

| Condition | Category |
|---|---|
| Pregnancy | NA |

**Clarification:** Use of PVRs is not required. There is no known harm to the woman, the course of her pregnancy, or the fetus if PVRs are accidentally used during pregnancy.

# NEW Recommendations for PVR

| Condition | Category |
|---|---|
| Breastfeeding ≥ 4 weeks | 1 |

**Clarification:** The woman must be actively breastfeeding (i.e. at least 4 breastfeeding episodes per day) during PVR use to maintain efficacy.

**Evidence**: No differences were observed between various measures of breastfeeding performance among PVR users compared with users of non-hormonal or progestogen-only (synthetic progesterone) contraceptives during 12 months of observation. No statistically significant differences in infant weight gain were observed among PVR users compared with women using a non-hormonal or progestogen-only contraceptives, and similar patterns of infant weight gain were observed in another study that compared PVR and IUD users. One study reported no significant difference in infant health.