



Progestin-only contraception (POC) Overview

An advanced slide kit complementing the
WHO training tool is available from
www.fptraining.org

This session discusses the most commonly used POCs in Europe

- Desogestrel 75 µg pill (POP)
- Drospirenone 4 mg pill (POP)
- Etonogestrel-releasing 3 year implant (Implant)
- Depot medroxyprogesterone acetate (DMPA)

Information about the levonorgestrel-releasing intrauterine system (LNG-IUS) will be given in the IUD/LNG-IUS sessions

Contents

- Progestin generations and properties
- Mechanisms of action
- Contraceptive efficacy and return to fertility
- Safety
- Use in women with medical conditions (incl. breastfeeding)
- Health benefits
- Contra-indications
- Adverse events: bleeding, breast tenderness, weight, acne, BMD

Progestins frequently used in POC Generation and some properties

Progestin	Generation	Anti-androgenic	Androgenic	Anti-mineralocorticoid	Glucocorticoid
Progesterone		(+)		(+)	
Levonorgestrel	2nd		+		
Desogestrel metabolite: etonogestrel	3rd		(+)		
Drospirenone	4th	+	-	+	-
Medroxyprogesterone acetate	Derived from progesterone		(+)		+

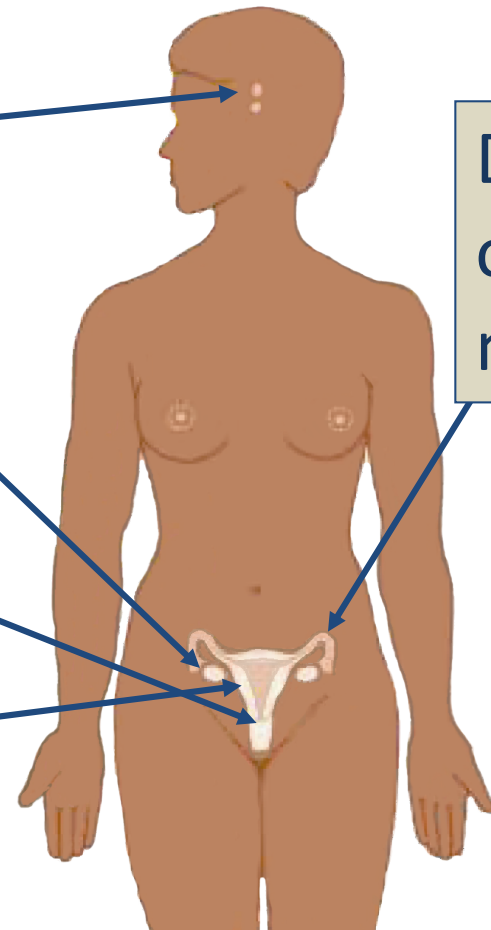
+, Strong binding; (+), less strong binding to the steroid receptor

POC (pill, implant, injectable) Mechanisms of action

Suppression of ovulation

Thickening of cervical mucus to block sperm

Endometrial effects



Decrease of tubal motility

Inhibition of ovulation is the key mechanism to prevent pregnancy

POC: Contraceptive efficacy

Method	% of women experiencing an unintended pregnancy within first year of use	
	Typical use	Perfect use
No method	85	85
Condom male	18	2
Combined pill	9	0.3
POP (DSG-DRSP)	9	0.7
Implanon	0.05	0.05
DMPA	6	0.2
IUD Copper T380Ag*	0.3	0.3
LNG-IUS 5 years*	0.2	0.2
Female sterilisation	0.5	0.5
Male sterilisation	0.15	0.1

*Source I.Sivin, Contraception 1990; Vol.42NO 4.; adapted from Trussell Contraception 2011;

POC: Return to fertility

- CHC: Immediate after last use
- POP: Immediate after last pill
- Implant: Immediate after removal
- DMPA: 6–9 months after last injection
- LNG-IUS: Immediate after removal

Return to fertility is delayed with DMPA

Safety

Venous thromboembolism

No increased risk of venous thromboembolism (VTE)

- POP users
- Implant users
- LNG-IUS users

- DMPA users

Very limited evidence suggests an increased odds ratio of VTE ($n=20$ cases)
After VTE or with thrombophilia: WHO MEC category 2

Safety

Stroke and myocardial infarction

No increased risk of stroke or myocardial infarction in:

- POP users
- Implant users
- LNG-IUS users

- **DMPA users: probably no increased risk**
- Little or no effect on glucose tolerance, but small increase in insulin levels
- Increase in LDL cholesterol and decrease in HDL cholesterol
- To date there are no epidemiological data indicating that these findings increase the risk of arterial thromboembolism (ATE)
- WHO MEC category 3 only if multiple cardiovascular risk factors are combined



POC is an important option
for women with medical conditions that do not allow use of (CHCs)

Medical condition	CHC	POP	Implant	Injectable	LNG-IUS
Postpartum (<21 days, no BF)	3-4	1	1	1	1-2*
Postpartum (21-42 days, no BF)	2-3	1	1	1	3*
Breastfeeding <6 weeks postpartum	4	2	2	3	3*
Breastfeeding 6 weeks-6 months pp	3	1	1	1	1
Smoking ≥ 35 years old	3-4	1	1	1	1
Multiple risk factors for arterial cardiovascular disease [#]	3-4	2	2	3	2
Diabetes (>20 years)	3-4	2	2	3	2
Diabetes with complications	3-4	2	2	3	2
Hypertension (sBP ≥160 mmHg or dBP ≥100 mmHg)	4	2	2	3	2
Thrombophilia	4	2	2	2	2
History of DVT/PE	4	2	2	2	2



Most important contraindications of POC

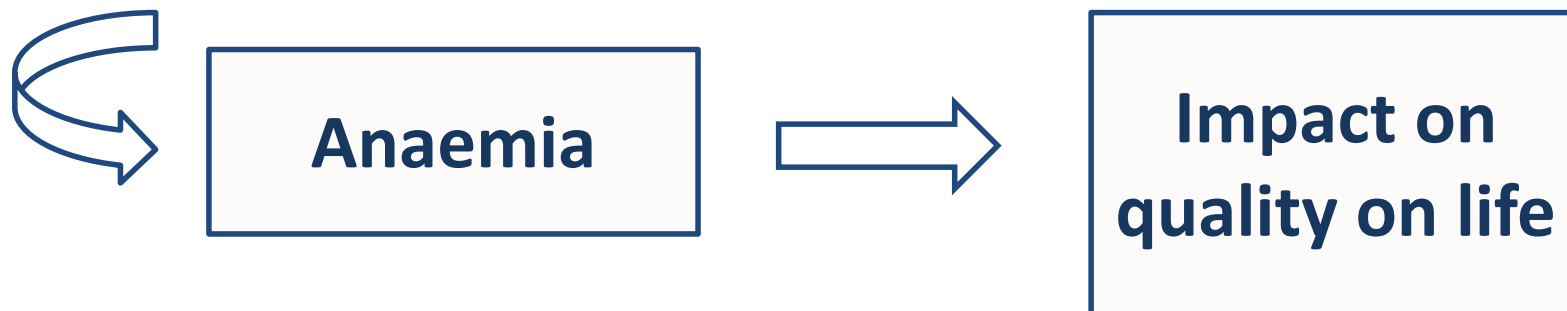
Medical condition	CHC	POP	Implant	Injectable	LNG-IUS
Acute DVT/PE	4	3	3	3	3
Unexplained vaginal bleeding	2	2	3	3	4
Severe liver disease	4	3	3	3	3
Malignant liver tumors	4	3	3	3	3
Current breast cancer	4	4	4	4	4
Past breast cancer (NED >5 years)	3	3	3	3	3

Health benefits of POC

- Reduction of heavy menstrual bleeding (HMB) (DMPA, LNG-IUS)
- Inhibition of growth of uterine fibroids (DMPA, LNG-IUS)
- Protection against iron-deficiency anaemia (DMPA, LNG-IUS)
- Reduction of sickle cell crises in women with sickle cell anaemia (DMPA)
- Reduction of dysmenorrhoea in women with endometriosis (POP, Implant, DMPA, LNG-IUS)
- Minimal metabolic effects (POP, Implant, LNG-IUS)
- Reduction of risk for endometrial cancer (DMPA)
- Positive impact on catamenial epilepsy*

POC for treatment of HMB

HMB: “The woman’s perspective of increased menstrual volume, regardless of regularity, frequency or duration”



The LNG-IUS and DMPA are the POC methods shown to be effective in the treatment of HMB

Adverse events of POC

Adverse events differ between POC methods, depending on dose, type of progestin and application


- Irregular bleeding/spotting, prolonged bleeding
- Amenorrhoea
- Weight gain
- Acne, hair loss
- Mood changes/depressed mood
- Decrease in Bone Mineral Density


Definitions of bleeding pattern (90 days)

Identify Your Flow


Visuals below may not apply to every woman's bleeding pattern.


Spotting

Spotting using Pad: 


Spotting using Tampon: 


Normal Bleeding

Medium Flow using Pad: 

Medium Flow using Tampon: 

Heavy Bleeding

Heavy Flow using Pad: 

Heavy Flow using Tampon: 

- **Frequent:** 5 or more bleeding episodes
- **Prolonged:** 1 or more bleeding episodes of >14 days
- **Infrequent:** Less than 3 episodes
- **Spotting:** Small amount of blood loss

Abnormal bleeding vs. amenorrhoea

- Uncomfortable changes in bleeding pattern and unpredictable bleeding are the main reason for discontinuation in POC users (23–30% in Europe)
- Many women would prefer amenorrhoea to unscheduled, prolonged or frequent bleeding

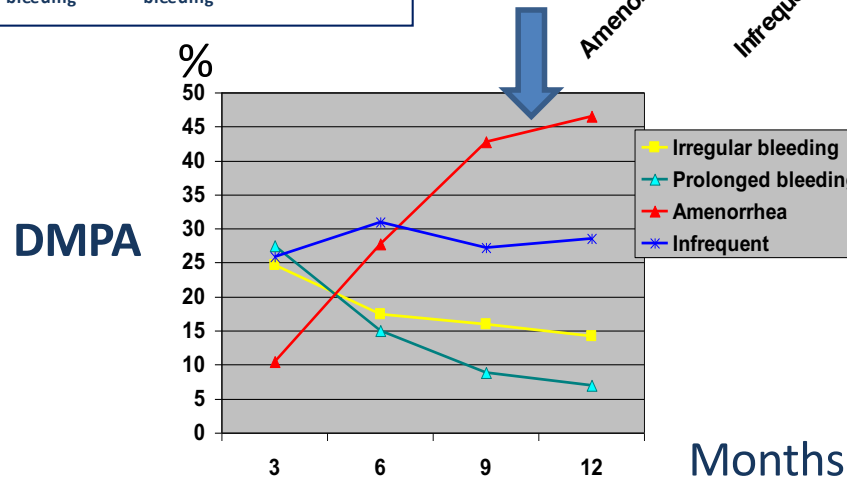
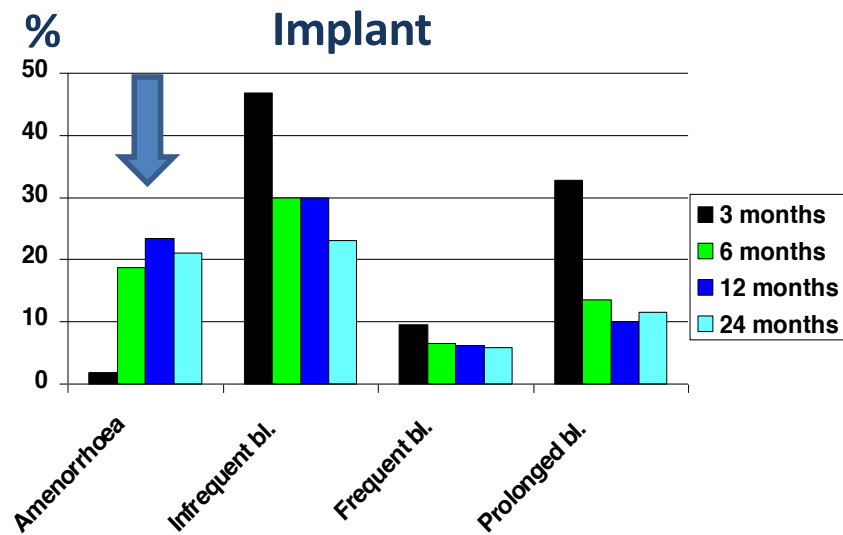
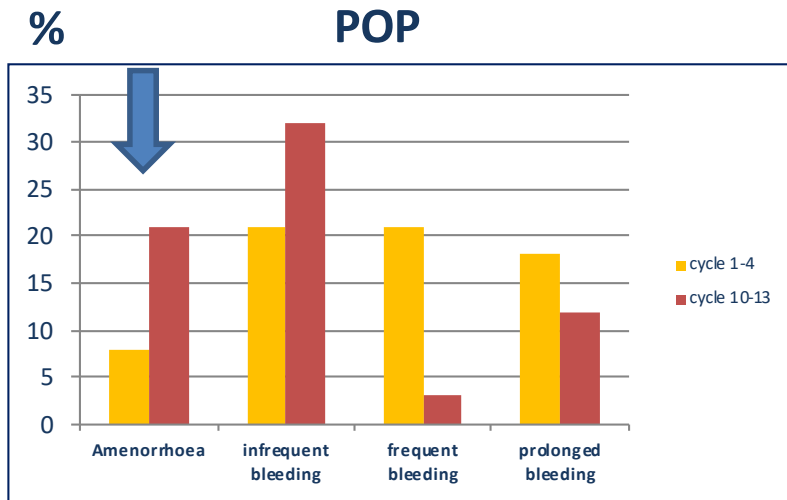


Bleeding pattern with POC methods

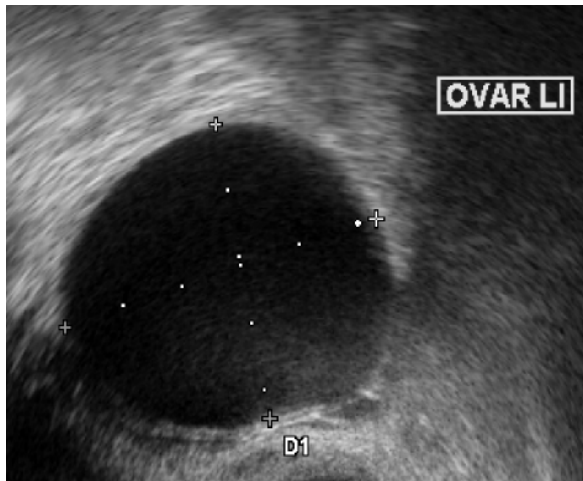
Method	Bleeding/spotting days over time	Amenorrhoea after 1st year
POP Desogestrel	Decreasing	20%
Implant	Decreasing	19–25%
DMPA	Decreasing	47–60%
LNG-IUS	Decreasing	43%

Frequency of frequent and prolonged bleeding decreases over time; therefore, reassurance is important if women find it troublesome

Amenorrhoea after 1 year: POP Desogestrel 20%; Implant 24%; DMPA i.m./s.c. 47–60%

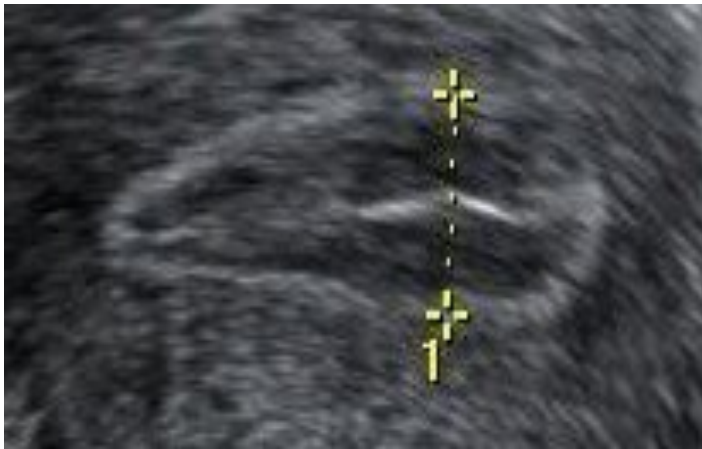


Breakthrough bleeding: by persistent unruptured follicles



- Reason for breakthrough bleeding (and breast tenderness) in users of very-low-dose POC ,such as the POP or the LNG-IUS, can be unruptured follicle cysts which produce estradiol
- These cysts resolve spontaneously
- Reassure the patient

Frequent and irregular bleeding: Treatment



If ultrasound is available, you can check whether the endometrium is high or low. Fragile vessels in atrophic endometrium will respond better to oestrogen treatment

Prolonged bleeding: Treatment options

- NSAIDs: ibuprofen 500–800 mg twice daily for 5 days
- Mefenamic acid 500 mg twice daily for 5 days
- Doxycycline twice daily for 5 days
- Tranexamic acid 500 mg twice daily for 5 days
- Norethisterone 5 mg 2–3 times daily for 21 days/2–3 cycles
- Estradiol 2 mg for 7 days or estradiol patch 50µg (if endometrium is atrophic) (if not contraindicated)
- CHCs for 21 days, if not contraindicated
- For DMPA, shorten interval between injections*
- Mifepristone (off-label)
- Ulipristal acetate 5 mg for 5 days

Bleeding pattern: How to counsel?

- It is very important to inform patients about the changes in bleeding pattern with POC use
- In many women the bleeding pattern (of the implant) over the first 6 months indicates the future bleeding pattern
- Support the woman to continue the method during that period
- Treatment mainly aims to stop uncomfortable, prolonged bleeding especially in the early phase of POC use
- There are no options to improve bleeding pattern in the long term

Counselling and continuation rates

- Good counselling is essential, but might not result in higher continuation rates if women continue to have an uncomfortable bleeding pattern
- One study reports that adequate counselling did not result in a lower discontinuation rate (53% at 2 years)
- In a randomised trial, routine counselling or intensive counselling had no effect on discontinuation rate due to unpredictable bleeding

Weight gain with POC methods



- POC methods exert different effects on weight
- Mean weight gain was <2 kg in most studies up to 12 months, and usually similar for the comparison group using another contraceptive
- 12 months POP data are limited, as the drop-out rate in the study was 45% (Ref 6)
- Clinical experience indicates discontinuation in some women because of weight gain



Weight gain compared with other contraceptives

Contraceptive method	Weight change (kg)	Percentage of women with particular weight increase
POP DSG (13 months)	No change	
Implant (24 months)	No change (31%) Increase >5 kg (20% W)	10% increase in body weight in 21% of users
DMPA (12 months)	2.4 kg	
DMPA (36 months)	5.8 ± (8.7) kg	20% increase >5 kg
DMPA (36 months)	3 kg	
LNG IUS (12 months)	1.03 kg	
Copper IUD (12 months) (36 months)	0.2 kg 0.6 kg	

A subgroup of women experiences a relevant increase of weight with use of the Implant and DMPA, what can result in discontinuation.

Acne, skin problems



A typical problem in adolescents, who are the biggest group of new contraceptive users

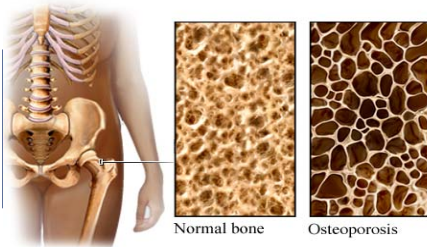
Acne and hair loss: Background

- Higher plasma levels of free testosterone contribute to androgenic side effects, such as acne and hair loss
- In contrast to CHCs, POCs do not increase and might even decrease sex hormone binding globulin (SHBG), the globulin that binds testosterone in blood
- Depending on the androgenic/antiandrogenic properties of the progestin in a POC, women may develop more or less acne
- Most studies report an incidence of acne of 7–17% with POC methods; however, these data are based on the subjective perception of the individual



Mood changes, depression

- POCs very rarely initiate depression in predisposed women (clinical report and some studies)
- POCs and progestin-releasing devices should not be initiated in women suffering from major depression (copper IUD might be a better alternative)
- If a woman complains of developing depressed mood while using POC, stop the method
- If no other option is available, inform the patient that mood can worsen and she should come back immediately if this happens (start a method which can easily be stopped)
- This is also true for the LNG-IUS
- For DMPA and DRSP evidence is lacking; therefore recommendations are based on clinical observations with all POC



Bone Mineral Density

- During the reproductive years maintenance of bone mineral density (BMD) is important to decrease fracture risk in later life
- Estrogen depletion can cause a decrease in BMD
- There is some concern that DMPA might have a negative impact on BMD by suppressing ovarian function
- Short-term studies do not indicate a negative effect of the desogestrel POP or implant on BMD
- For the DRSP POP no prospective data are available yet

POC: Summary (1)

Advantages

- High efficacy
- Efficacy not user-dependent (except POP)
- No increase in VTE or ATE risk (DMPA WHO 2-3)
- Minimal metabolic effects
- No adverse effects of ethinyl-estradiol
- Safe in many medical conditions
- Improvement of HMB (DMPA, LNG-IUS)
- No negative impact on lactation

POC: Summary (2)

Disadvantages

- Unpredictable/prolonged bleeding
- Impact on body weight in some women
- Hormonal side effects (skin, hair)
- Negative, but probably reversible, impact on bone density with DMPA
- Return to fertility delayed with DMPA
- Impact on mood, especially in predisposed women