# Combined hormonal contraceptives CHC Session III

Advanced slide kit complementing the WHO training tool www.fptraining.org

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# Noncontraceptive health benefits of CHCs

- Decrease in dysmenorrhoea
- Decrease in intensity and duration of bleeding
- Less iron-deficiency anaemia
- Possibly less benign breast disease
- Less endometriosis
- Less ovarian cysts with COC containing 30µg EE
- Decreased risk of endometrial and ovarian cancer
- Probably lower incidence of colon cancer
- Maintenance of bone density

Ref 1

# Minor harmless side effects Frequency in CHC users

| | Frequency in % |
|---|---|
| **Breast tension** | 3-12 |
| **Headache** | 6-14 |
| **Nausea** | 3-7 |
| **Abdominal pain** | 2-3 |
| **Libido problems** | 1-3 |
| **Nervous mood** | 1-3 |
| **Depressive mood** | 1-3 |
| **Acne** | 3-15 |

Ref 1-6

# Minor harmless side effects

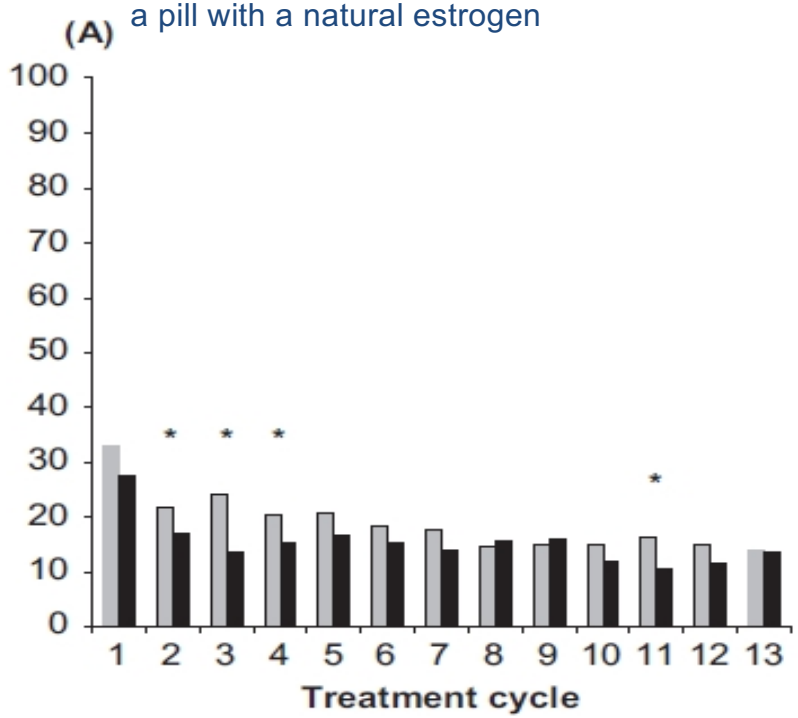
In placebo-controlled trials headache, nausea and breast discomfort occurred at the same rate in both groups (1)

Harmless side effects should be treated if they continue for more than 3 months and are disturbing for the woman. One option is to change the estrogen dose or the progestin type in the CHC. Sometimes switching to another form of application is helpful.

Ref 1

# Minor adverse events
## Unscheduled bleeding in Newstarters

Incidence of breakthrough bleeding using a pill with ethinylestradiol or a pill with a natural estrogen

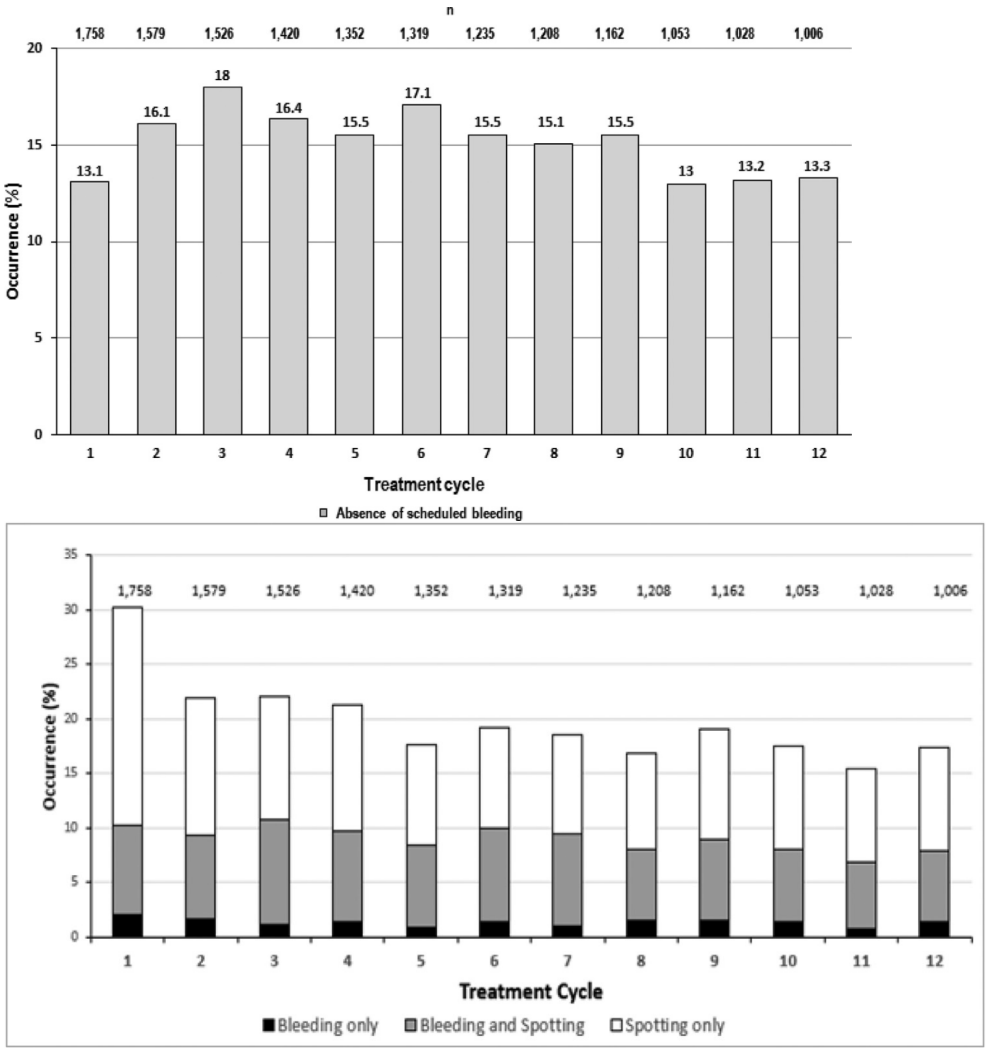



Black bars, EE 30 µg/drospirenone; grey bars, estradiol/nomegestrol acetate (*$p$<0.05 vs EE/ drospirenone). Adapted from Ref 3.

- The incidence of breakthrough bleeding in the first 3 months of CHC use ranges from 10-30%. Patients should be told that breakthrough bleeding is harmless and does not affect efficacy.
- Breakthrough bleeding is more frequent with lower dose pills (< 30 µg EE) and with pills containing E2, EV and E4.*
- If these bleedings do not stop and are disturbing, increase estrogen dose (but not above 35 µg EE), change to a stronger progestin like desogestrel, gestoden or dienogest, or switch to the vaginal ring.

Ref 1-5

# E4 /DRSP bleeding pattern




Percentage of participants with unscheduled bleeding and/or spotting per cycle up to 13 cycles ∗. The number of cycles at the top represents the number of participants starting each cycle. ∗Cycle 13 data are not reported here since the last 3 days of scheduled bleeding in Cycle 13 (i.e., Days

Absence of scheduled bleeding occurs on the long-term in around 13% of the cycles

Unscheduled bleeding occurs on the long-term in around 16% of the cycles

Ref. 1

# Minor adverse events – Treatment Unscheduled bleeding

**Exclude the following causes**

- Irregular pill intake
- Vomiting (pill)
- Co-medication with enzyme inducing drugs or St. John's worth
- Chlamydia infection
- Organic causes: colposcopy, Pap smear, endometrial or ovarian ultrasound

- Advice: no reason to stop the method, but change the compound, if the user finds the breakthrough bleeding troublesome.
- No effect on efficacy if pill was taken correct (7 days rule)!

# Minor adverse events - Treatment Headache

- Exclude migraine: If headaches are migraines and were not mentioned in the history, or were mentioned but are now more frequent, recommend to change to a method without estrogen.
- Exclude change from migraine without aura to migraine with aura.
- If headaches occur mainly during the pill break, consider a EV/Dienogest pill 26/2 regimen or a 24 /4 regimen with 15 µg EE (Ref 1).
- Decreasing the estrogen dose or change to another progestin might help.

Ref 1

# Minor adverse events - Treatment altered mood, irritability

- Irritability, nervousness, despondence – consider increasing estrogen or changing the progestin
- If problems arise mainly during pill break, switch to a 24/4 or 26/2 regimen with less intense hormonal withdrawal

Evidence low

# Minor adverse events - Treatment Breast tenderness

**In newstarters**

- Decrease the estrogen dose or change to a progestin with antimineralocorticoid effect (drospirenone)
- If this symptom occurs in users of a very low dosed pill (20µg EE or less) increase the estrogen dose (note)
- If this is not successful change to POC or IUD

**In long-term users**

- Exclude organic causes (prolactin, thyroid)
- Consider to change to an estrogen-free method

Evidence low

# Minor adverse events - Treatment Low libido

Low libido is mostly associated with relationship issues. Before changing hormones try to discuss the following:

- Has sexual behaviour changed since starting the pill?
- Does the patient suffer from vaginal dryness or pain?
- What is considered normal by the couple?
- Is one of the partners in a stressful situation at work or privately?
- In postpartum situations exclude stress factors such as lack of sleep and mood problems.
- **If problems can be attributed to the pill try to use a more androgenic progestin (levonorgestrel**) or switch to a non-hormonal method.

# Effect of CHCs on weight after 13 cycles of use

- **Low dose CHCs do not typically cause weight gain**
- No differences are found in weight change between users of CHC with 15 µg EE, 20 µg EE or 30 µg EE
- After 13 cycles of CHC use weight change within ± 2 kg was observed in 65-81% of users
- Weight increase of more than 2 kg is found in around 11% of CHC users, however reasons are difficult to define (pill use vs other reasons)
- Weight loss of 2 kg has also been found in around 11% of CHC users

Discuss eating habits, hours of physical training, more appetite. Changing to another progestin might help in some cases, but there is no clear evidence for this. Drospirenone decreases water retention if this is the problem.

Ref 1

# Major adverse events
# Breast cancer risk in current and recent CHC users

## Study population 15-49 year old women

| | Incidence/100.000 | Relative risk |
|---|---|---|
| Non-users | 55 | 1.00 |
| | Additional cases in numbers/100.000 | |
| Previous users | +3 (1-6) | 1.08 |
| Current and recent users | +13 (10-17) | 1.19 |

Ref 1

# Major adverse event
# Breast cancer risk in current and recent CHC users

## Study population 15-49 year old women

| Duration of use | Number of additional events/100.000 person-years | Relative risk |
|---|---|---|
| <1 year | -1 (-8-8) | 1.03 ns |
| 1-<5 years | 9 (3-14) | 1.17 s |
| 5-10 years | 15 (8-21) | 1.27 s |
| >10 years | 21 (14-28) | 1.46 s |

Ref 1

# Major side effects Breast cancer

- This increase of breast cancer risk has to be balanced against the protective effects of CHC on ovarian, endometrial and colon cancer
- Data are insufficient for preparations with estradiol, estradiol-valerate, estetrol, the CVR and the CTP
- Data are insufficient to recommend preferred prescription of any type of progestin in COC or POC (including LNG-IUS)

Ref 1

# Major side effects / depression

**Women with a first diagnosis of depression**:

Non-HC users 2.8 /1.000 wy

HC users 3.0/1.000 wy

This corresponds with 2 more cases of depression in 10.000 women using HC

| | |
|---|---|
| CHC users | RR 1.1 s |
| CHC users adolescence | RR 1.7 s |

The study has relevant weaknesses*

Ref 1

# Major side effects / depression

Conclusions

- The number of additional depressions in HC users is very low (2/10.000)
- Most depressions start within the first 6 months of use
- If a new depression is observed in HC newstarters, the HC could be the cause and therefore should be stopped
- Risk and benefit of newstart of any type of HC in the later future has to be discussed with the psychiatrist

Ref 1

# Major side effects / Reasons to stop pill immediately

# Stop the pill and seek urgent advice from your doctor if you notice any of the following symptoms

- Weakness of arm, leg
- Numbness of the face, arm or leg
- Severe unilateral, pulsating headache with paresthesia or visual symptoms
- Severe pain or swelling in the legs
- Sudden, unexplained breathlessness
- Rapid breathing or cough
- Chest pain
- Jaundice

# VTE risk in newstarters

| **Adapted from (1) (3)** | **Newstarter**<br>**< 1 years (Ref1)**<br>**< 1 years (Ref3)** | **Long-term user**<br>**> 4 years (Ref 1)**<br>**> 5 years (Ref 3)** |
|---|---|---|
| | Odds ratio | Odds ratio |
| Non-use | 1 | 1 |
| CHC use | 4-9 | 2-6 |

The VTE risk is very high in newstarters especially during the first three months (OR 12.6) and the first year of use. It therefore makes sense to increase awareness for symptoms in patients and doctors (Ref 2)

Ref 1-3

# If a cardiovascular event occurs you will in many cases reduce longterm impact on your health if you see a doctor soon enough

# European Medicines Agency (EMA) recommends to inform patient about cardiovascular symptoms

Do not delay diagnosis of VTE or PE in CHC users!

Early diagnosis of VTE, LE and stroke improves prognosis and reduces complications. As new users in particular are affected, symptoms they must watch out for should be described during counselling.

Ref 1

# The Pill return visit in newstarters after three months

- Many women might not ask for an appointment if they have only minor side effects or questions arising with daily use of the pill. Nevertheless they might be worried and stop the pill at a certain point.
- A planned visit three months after starting the pill and after counselling is a good option to intervene in cases of side effects, exclude problems with regular pill use and measure blood pressure.