Combined hormonal contraceptives
CHC Session III

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

Update March 2019
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When talking about CHC it should not be forgotten that in addition to providing contraception this contraceptive method is associated with additional health benefits. These benefits can be used to treat gynaecological problems and disorders.

Risk reduction in ovarian cancer with modern CHC: (Ref 1) Among ever users of hormonal contraception, the reduction in the age standardised absolute rate of ovarian cancer was 3.2 per 100 000 person years. Based on the relative risk for the never use versus ever use categories of hormonal contraception (0.66), the population prevented fraction was estimated to be 21%—that is, use of hormonal contraception prevented 21% of ovarian cancers in the study population. The reduction in ovarian cancer risk in women of reproductive age—an effect related to duration of use and diminishes after stopping use. The data suggest no protective effect from progestogen-only products, but the observed person years for these products were small.
• There are no visible differences between pills containing 30 µg or 20 µg EE with regard to these side effects.
When discussing harmless side effects after starting a CHC, inform the patient that typically those symptoms will disappear within 3 months of use. Placebo-controlled studies found similar numbers of women with nausea, headache or breast discomfort in both the placebo and treatment groups. Side effects can be troublesome in daily life and should therefore be treated. Most recommendations for the treatment of side effects are based on clinical experience.


Unscheduled bleeding (defined as bleeding/spotting episodes not starting in the pill-free interval) is common in CHC newstarters and decreases with longer duration of use. COC with 20 µg EE are associated with more breakthrough bleeding than those with 30 µg EE.

- In COCs containing natural estrogens, breakthrough bleeding is common even in long-term users.
- If pills have been taken correctly, unscheduled bleeding does not indicate decreased efficacy.
- In long-term users with a normal bleeding pattern, new breakthrough bleeding may indicate chlamydia infection.
Unscheduled bleeding is uncomfortable and irritating. You should therefore discuss changing to another CHC after other causes of breakthrough bleeding have been excluded. The vaginal ring has a very stable bleeding pattern.
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
Breast tenderness and ovarian cysts in users of very-low-dose pills can be caused by diminished suppression of follicular activity in the ovary. Estrogens produced in the ovary combine with estrogens in the pill to cause breast tenderness.
If vaginal dryness is a problem a lubricant may help.
1. Hâni, D. Merki-Feld G.S.: Weight gain due to hormonal contraception: myth or truth? Gynäkologische Rundschau 2008;87-93
Background:

- nationwide prospective cohort study involving all women in Denmark between 15 and 49 years of age.
- 1.8 million women were followed on average for 10.9 years (a total of 19.6 million person-years), 11,517 cases of breast cancer occurred.
- As compared with women who had never used hormonal contraception, the relative risk of breast cancer among all current and recent users of hormonal contraception was 1.20 (95% confidence interval [CI], 1.14 to 1.26).
- After discontinuation of hormonal contraception, the risk of breast cancer was still higher among the women who had used hormonal contraceptives for 5 years or more than among women who had not used hormonal contraceptives.
- Use of the LNG-IUS was also associated with an increased risk (relative risk, 1.21; 95% CI, 1.11 to 1.33).
- The overall absolute increase in breast cancer diagnosed among current and recent users of
any hormonal contraceptive was 13 (95% CI, 10 to 16) per 100,000 personyears.
### Major adverse event

Breast cancer risk in current and recent CHC users

Study Population: 15-49 year old women

<table>
<thead>
<tr>
<th>Duration of use</th>
<th>Number of additional events/100,000 person-years</th>
<th>Relative risk</th>
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<tbody>
<tr>
<td>&lt;1 year</td>
<td>-1 (-8-8)</td>
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<tr>
<td>1-&lt;5 years</td>
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<td>5-10 years</td>
<td>15 (8-21)</td>
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<td>&gt;10 years</td>
<td>21 (14-28)</td>
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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 or estradiolvalerate, 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 2.8/1000 wy
HC users 3.0/1000 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*


- Nationwide prospective cohort study combined data from the National Prescription Register and the Psychiatric Central Research Register in Denmark. All women and adolescents aged 15 to 34 years who were living in Denmark were followed up from January 1, 2000, to December 2013, if they had no prior depression diagnosis, redeemed prescription for antidepressants, other major psychiatric diagnosis.
- RESULTS A total of 1 061 997 women (mean [SD] age, 24.4 [0.001] years; mean [SD] follow-up, 6.4 [0.004] years) were included in the analysis.
- Compared with nonusers, users of combined oral contraceptives had an RR of first use of an antidepressant of 1.23 (95%CI, 1.22-1.25).
- Users of progestogen-only pills had an RR for first use of an antidepressant of 1.34 (95%CI, 1.27-1.40);
- users of a levonorgestrel intrauterine system, 1.4 (95%CI, 1.31-1.42).
• For depression diagnoses, similar or slightly lower estimates were found.
• The relative risks generally decreased with increasing age.
• Adolescents (age range, 15-19 years) using combined oral contraceptives had an RR of a first use of an antidepressant of 1.8 (95%CI, 1.75-1.84) and those using progestin-only pills, 2.2 (95%CI, 1.99-2.52).
Limitations and not considered points:

• Background of control group with information on sexual activity of included women and contraception used is missing
• Family history is not known (increases Risk 2.8 fold)
• Antidepressants are prescribed for many psychiatric diagnosis not only depression
• Adolescence is a typically age for newstart of depressions
• First partnership and first intercourse might be a demanding situation for some adolescents
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
If a cardiovascular event occurs you will in many cases reduce long-term impact on your health if you see a doctor soon enough.
1. Source: European Medicines Agency: Information for patients: When taking CHCs, you should be alert for the signs and symptoms of blood clots, which may include severe pain or swelling in the legs, sudden unexplained breathlessness, rapid breathing or cough, chest pain, and weakness or numbness of the face, arm or leg. If you develop any of these signs and symptoms you should seek medical advice immediately.

**Conclusion Ref 1**: Fair-quality evidence from five reports showed that women who did not have their blood pressure measured prior to COC initiation had a higher risk of acute MI and ischaemic stroke compared with women who did have their blood pressure measured. One study with fair-quality evidence showed no increased risk of haemorrhagic stroke based on whether or not blood pressure was measured. Studies that examined hormonal contraceptive methods other than COCs were not identified.

Reasons to recommend a follow-up visit especially in new users include the opportunity to:

- Establish that the patient is using the pill correctly
- Discuss any problems with pill use
- Discuss any ongoing side effects (to encourage continuation)
- Check blood pressure
- Talk about STIs and condoms
- Check for warning signs such as new migraine