Avon CASH Contraception Meeting January 2019

Combined Hormonal Contraception Cases

Case 1

Bridget (Jones) a 43 year old first time mum comes to see you 4 weeks after the delivery of her baby boy.

She had a difficult pregnancy and delivery and is desperate to start contraception straight away as she is very sure she doesn't want to get pregnant again.

She really wants to start the combined oral contraceptive pill again – she has taken it in the past and loved it!

She is not breastfeeding. She had a vaginal delivery, but had a postpartum haemorrhage and needed a 2 unit blood transfusion.

She has put on a bit of weight during pregnancy and her BMI is 32.

What else do you want to know?

Would you consider prescribing her CHC now?

If so what pill would you choose?

What should you inform Bridget about the COCP?

Facilitator notes:

Ask Bridget:

Medical and Family History

Drug History

Smoking – and if ex smoker – when did she give up??

BP and BMI

Any reasons why CHC may be contra indicated or less effective?

UKMEC for CHC:

Smoking		
a) Age <35 years	2	**Clarification:** UKMEC currently does not include use of e-cigarettes, as risks associated with their use are not yet established. **Evidence**: COC users who smoke are at an increased risk of CVD, especially MI, compared with those who do not smoke. Studies also show an increased risk of MI with an increasing number of cigarettes smoked per day. [23–34] The 35 year age cut off is identified because any excess mortality associated with smoking becomes apparent from this age. [35] The mortality rate from all causes (including cancers) decreases to that of a non-smoker within 20 years of smoking cessation. The CVD risk associated with smoking decreases within 1 to 5 years of smoking cessation. [35–37]
b) Age ≥35 years		
(i) <15 cigarettes/day	3	
(ii) ≥15 cigarettes/day	4	
(iii) Stopped smoking <1 year	3	
(iv) Stopped smoking ≥1 year	2	
Obesity		**Clarification:** The absolute risk of VTE in women of reproductive age is low. The relative risk of VTE increases with CHC use. Nevertheless, the absolute risk of VTE in CHC users is still low. **Evidence:** The risk of VTE rises as BMI increases over 30 and rises further with BMI over 35. Use of CHC raises this inherent increased risk further. [28,34,38–41] Limited evidence suggests that obese women who use COC do not have a higher risk of acute MI or stroke than obese non-users. [34,42–44]
a) BMI ≥30–34 kg/m^2	2	
b) BMI ≥35 kg/m^2	3	

UKMEC for CHC and post partum:

Note new category (with most recent UKMEC and postnatal guidelines) of introducing concept of if patient has additional risk factors for VTE.

Pregnancy	NA	**Clarification:** There is no known harm to the woman, the course of pregnancy or the fetus if CHC is accidentally used during pregnancy.
Age		
a) Menarche to <40 years	1	
b) ≥40 years	2	**Clarification:** Guidance from the FSRH supports use of CHC up to age 50 years if there are no medical contraindications to use. [2]
Parity		
a) Nulliparous	1	
b) Parous	1	
Postpartum (in breastfeeding women)		**Evidence**: One systematic review reports that the impact of COC on breastfeeding duration and success is inconsistent. Results are conflicting on whether early initiation of COC affects infant outcomes, but generally find no negative impact on infant outcomes with later initiation of COC. [3]
a) 0 to <6 weeks	4	
b) ≥6 weeks to <6 months (primarily breastfeeding)	2	
c) ≥6 months	1	
Postpartum (in non-breastfeeding women)		**Clarification:** This includes any births, including stillbirths from 24 weeks gestation. **Clarification**: In the presence of other risk factors for VTE, such as immobility, transfusion at delivery, BMI ≥30 kg/m^2, postpartum haemorrhage, immediately post-caesarean delivery, pre-eclampsia or smoking, use of CHC may pose an additional increased risk for VTE. **Evidence**: VTE risk is elevated during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, declining to near baseline levels by 42 days postpartum. [4–8] Use of CHC, which increase the risk of VTE in women of reproductive age, may pose an additional risk if used during this time. [9] Risk of pregnancy during the first 21 days postpartum is very low, but increases after that time in non-breastfeeding women; ovulation before first menses is common. [10]
a) 0 to <3 weeks		
(i) With other risk factors for VTE	4	
(ii) Without other risk factors	3	
b) 3 to <6 weeks		
(i) With other risk factors for VTE	3	
(ii) Without other risk factors	2	
c) ≥6 weeks	1	

Postpartum
Use of combined hormonal contraception (CHC) by women following childbirth

The UKMEC table (Section B) for CHC/ postpartum (in non-breastfeeding women) notes that:

VTE risk is elevated during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, and then declines rapidly to near baseline levels by 42 days postpartum. In the absence of other risk factors, it is acceptable to prescribe CHC after 3 week postpartum in non-breastfeeding women.

Use of CHC may pose an additional increased risk for VTE in the presence of other risk factors for VTE, such as immobility, transfusion at delivery, BMI ≥30 kg/m2, postpartum haemorrhage, immediately post-caesarean delivery, pre-eclampsia or smoking. See method section of UKMEC for clarification/ evidence.

As Bridget is between 3-6 weeks postpartum and with additional risk factors for VTE (BMI > 30, postpartum haemorrhage and blood transfusion) = UKMEC 3 for CHC now.

Providing Bridget has no other reasons that would CI her to CHC she could start the CHC at 6 weeks post partum.

BMI 30 - 34 = UKMEC 2

She would need to be made aware that there are other safer and more effective forms of contraception than CHC.

But it is about patient choice and she can use it if she wants > 6 weeks post partum.

Could therefore use a bridging method of contraception e.g. POP until 6 weeks post partum.

She would need to be told about CHC:

1. Effectiveness:

Perfect use < 1% failure

Typical use 9% estimated failure

Explain factors that affect effectiveness

2. Risks of significant adverse health events associated with CHC use is small, but…

   Many health risks are greater with CHC than with progestogen-only/ non-hormonal contraception.

   CHC related health events can be very serious

   UKMEC 2016 guides safe CHC use (recommendations are unchanged)

   CHC use can be considered menarche to age 50

   But background risk of adverse health events increases significantly with age.

   Risks – VTE, MI, Ischaemic stroke
   Risks – Ca Breast and cervix

VTE:

Risk during use x 3-5 compared to non use

Absolute numbers small (5-12 per 10,000 CHC users / year)

1% fatal

CHC use lower risk of VTW than pregnancy

But Safer options of contraception available.

ATE:

Risk during use x 1.6 (MI) and x 1.7 (CVA)

Absolute numbers small (approx. 2.1 thrombotic strokes and 1 MI per 10,000 CHC users / year)

Risks increase with BMI, Smoking, BP etc

Ca Breast:

Risk x 1.2 (estimates vary) during current use

Risk decreases over time after stopping – no increased risk after 10 years of stopping.

Incidence:
Aged 20-24 = 0.1 per 10,000

Aged 45-49 = 22 per 10,000

Ca Cervix:

Risk x 2 approx with 5 years of use

Risk decreases after stopping CHC

Discuss / Give patient list of signs / symptoms that mean should seek medical attention (see FSRH guideline and below photo).

3. Benefits:
    - reduction in ovarian and endometrial cancer and colorectal cancer.
    - Other non-contraceptive benefits – help with period problems, pms, endometriosis, acne etc…

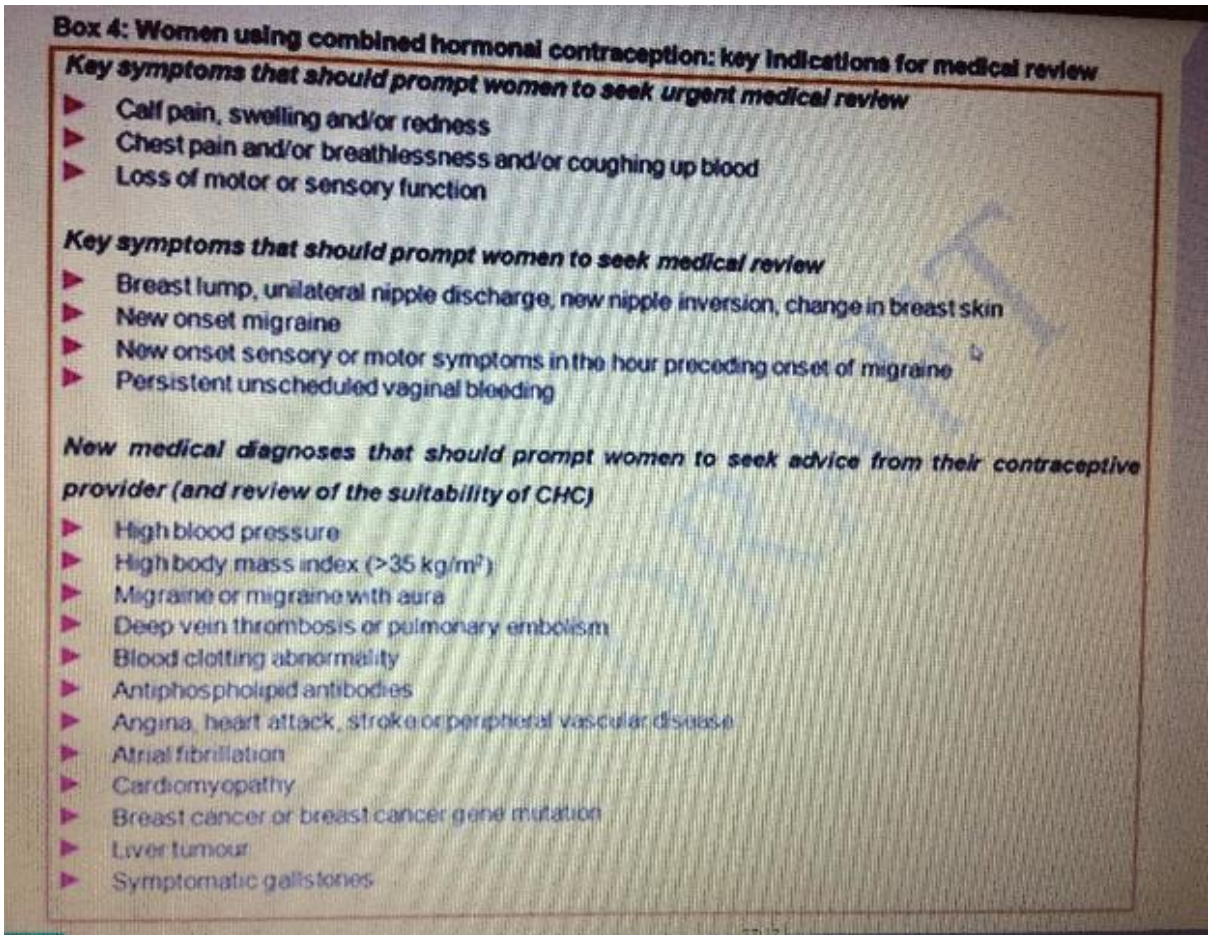
4. Possible side effects.
5. How to use and what to do if use incorrect.
6. Discuss / offer appropriate alternative methods (including LARC).

Choice of CHC:

COC containing </= 30 mcg EE in combination with levonorgestrel or norethisterone is first line choice of CHC to minimise cardiovascular risk.

Still no evidence that estradiol (E2) COC is safer than EE (ethinyl estradiol).

Pill vs Patch vs Ring – dependent on patient preference.



Box 4: Women using combined hormonal contraception: key indications for medical review

Key symptoms that should prompt women to seek urgent medical review

- Calf pain, swelling and/or redness
- Chest pain and/or breathlessness and/or coughing up blood
- Loss of motor or sensory function

Key symptoms that should prompt women to seek medical review

- Breast lump, unilateral nipple discharge, new nipple inversion, change in breast skin
- New onset migraine
- New onset sensory or motor symptoms in the hour preceding onset of migraine
- Persistent unscheduled vaginal bleeding

New medical diagnoses that should prompt women to seek advice from their contraceptive provider (and review of the suitability of CHC)

- High blood pressure
- High body mass index (>35 kg/m^2)
- Migraine or migraine with aura
- Deep vein thrombosis or pulmonary embolism
- Blood clotting abnormality
- Antiphospholipid antibodies
- Angina, heart attack, stroke or peripheral vascular disease
- Atrial fibrillation
- Cardiomyopathy
- Breast cancer or breast cancer gene mutation
- Liver tumour
- Symptomatic gallstones

Case 2

Bridget's friend Shazzer comes to your evening clinic. She has run out of her COCP, Marvelon. She should have started it yesterday morning but couldn't get time off work sooner to get her repeat prescription. She is now 36 hours late in restarting her pill packet.

What do you want to ask Shazzer?

What should you advise her about starting her COCP again?

Facilitator Notes:

Has Shazzer had UPSI during the HFI?

If she has had UPSI she should be offered emergency contraception as HFI > 7 days.

Either:

Levonelle and then can quick start COCP immediately.

COCP will be effective after 7 days.

Patient will need to do repeat PT in 3 weeks (irrespective of bleeding pattern – as withdrawal bleed not a reliable indicator that not pregnant).

Or

EllaOne and delay starting COCP for 120 hours.

COCP will still take 7 days to become effective.

Patient will need to do PT in 3 weeks.

Or

PC Cu IUD – can be fitted up to day 13 of HFI

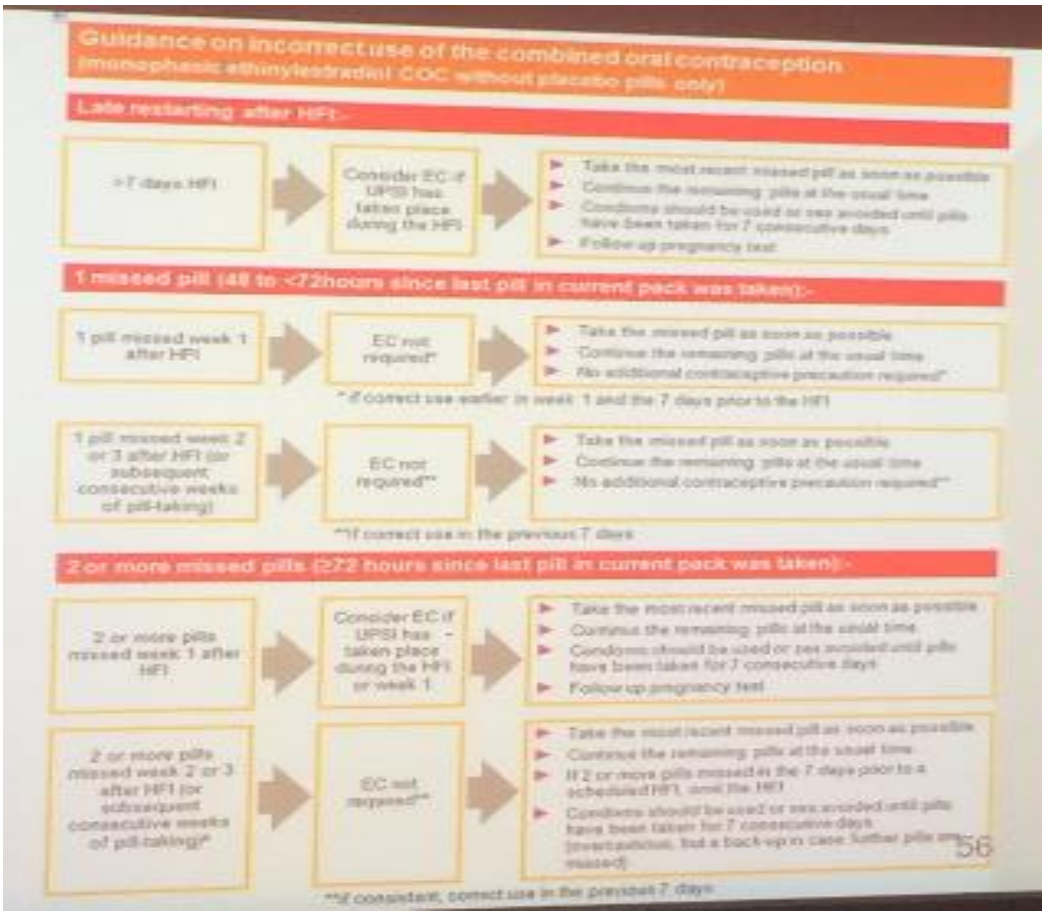
Earliest observed ovulation was day 8 of HFI in 1 study (see below) – most ovulation was seen much later than day 8 of HFI.

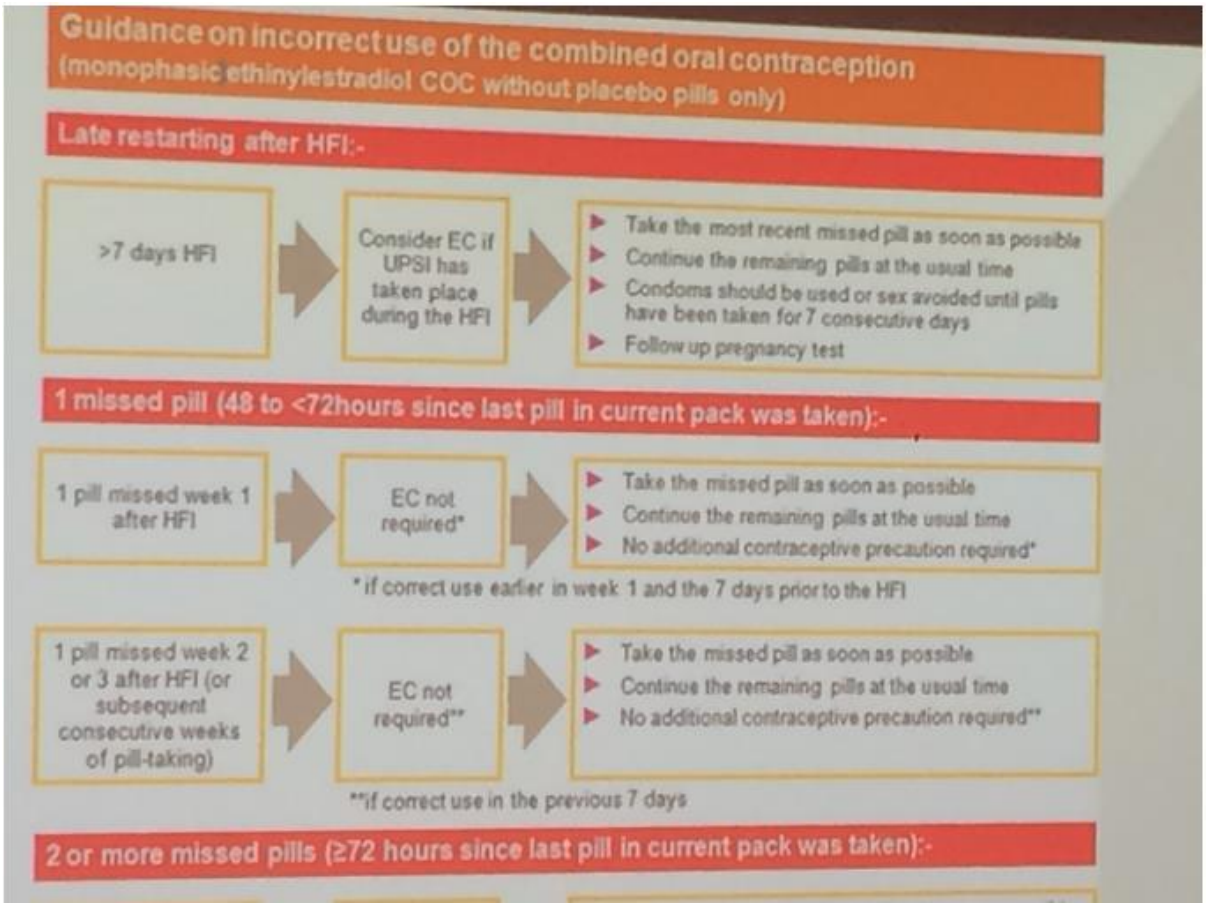
Therefore if UPSI latest a PC IUD can be fitted is day 13 of HFI = before earliest possible date of implantation.

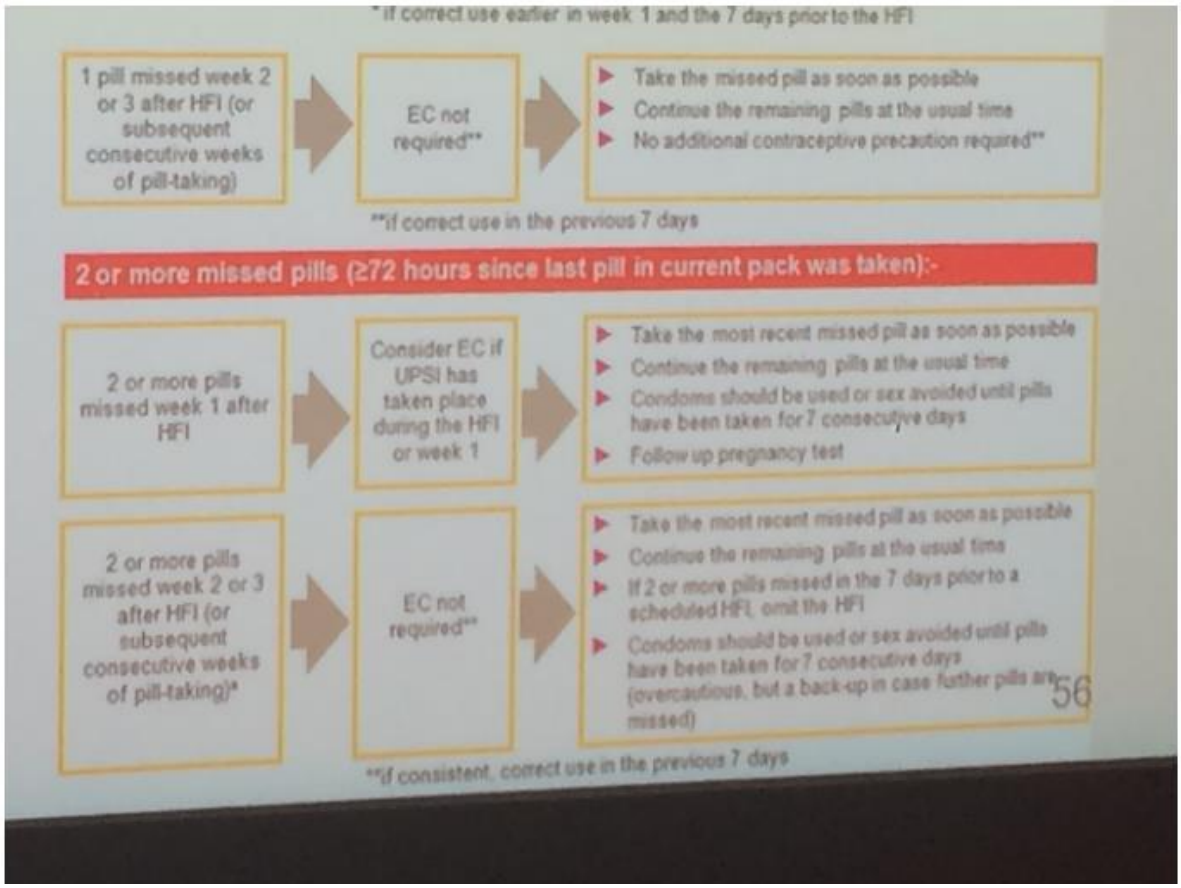
New Missed pill rules being developed separately by FSRH.

Interim guidance – chart published with guideline and on webinar:

From CHC webinar:




Guidance on incorrect use of the combined oral contraception
(monophasic ethinylestradiol COC without placebo pills only)
Late restarting after HFI:-
>7 days HFI
Consider EC if UPSI has taken place during the HFI
Take the most recent missed pill as soon as possible
Continue the remaining pills at the usual time
Condoms should be used or sex avoided until pills have been taken for 7 consecutive days
Follow up pregnancy test
1 missed pill (48 to <72hours since last pill in current pack was taken):-
1 pill missed week 1 after HFI
EC not required*
Take the missed pill as soon as possible
Continue the remaining pills at the usual time
No additional contraceptive precaution required*
* if correct use earlier in week 1 and the 7 days prior to the HFI
1 pill missed week 2 or 3 after HFI (or subsequent consecutive weeks of pill-taking)
EC not required**
Take the missed pill as soon as possible
Continue the remaining pills at the usual time
No additional contraceptive precaution required**
**if correct use in the previous 7 days
2 or more missed pills (≥72 hours since last pill in current pack was taken):-



From FSRH EC Guideline:

Cu-IUD insertion for EC after incorrect use of CHC

Ovulation may occur if CHC is used incorrectly during Week 1 of pill/patch/ring or if the hormone-free interval (HFI) is extended.

Timing of ovulation after missed pills or detached/removed combined contraceptive patch or ring during Week 1 cannot be predicted for each individual case. Non-compliance with CHC in Week 1 should therefore be considered an extension of the HFI.

A systematic review of studies considering ovulation after an extended HFI in users of combined oral contraception (COC) reports the earliest ovulation at 8 days after the last correctly taken pill in the previous pill packet.[73]

The largest study included 99 women randomised to one of three treatment groups (i.e. very low-dose monophasic desogestrel, low-dose monophasic gestodene or triphasic gestodene COC), all of which included one cycle of extending the HFI to 10 days. No ovulations and one luteinised unruptured follicle were reported in 98 cycles.

A small study (n=15) reported the earliest ovulation after a HFI of 13 days in users of the combined vaginal ring. No data are available for ovulation after an extended HFI amongst users of the combined transdermal patch.[73]

Based on the fact that the earliest observed ovulation occurred 8 days after stopping CHC (the majority occurred significantly later), the GDG recommends that a Cu-IUD can be inserted for EC up

to 13 days after the start of the HFI, provided that the combined hormonal method was used correctly prior to the HFI. This ensures that the Cu-IUD is inserted prior to implantation, even in the unlikely event that ovulation occurs 8 days after stopping CHC.

Note:

New Guideline supports up to 1 year supply of new or repeat CHC – at the discretion of prescriber – useful for patients with Normal BP, BMI and no medical conditions.

This may reduce risk of patients running out of supplies.

New Guideline also supports use of remote or online prescribing of CHC – providing robust way of reviewing medical history (consider use of validated patient completed questionnaires) and up to date BP and BMI – could this be done by machine elsewhere (pharmacy or in waiting room at clinic).

Table 1: Indications for emergency contraception following potential failure of hormonal and intrauterine methods of contraception (see Section 13.2 for clarification)

Method	Situation leading to possible contraceptive failure	Indication for EC
Hormonal methods of contraception	Failure to use additional contraceptive precautions when starting the method	UPSI or barrier failure during time that additional precautions required as indicated within CEU guidance.
Combined hormonal transdermal patch or combined hormonal vaginal ring	Patch detachment/ring removal for >48 hours Extension of patch-free or ring-free interval by >48 hours	EC is indicated if patch detachment or ring removal occurs in Week 1 and there has been UPSI or barrier failure during the hormone-free interval (HFI) or Week 1. If the HFI is extended, a Cu-IUD can be offered up to 13 days after the start of the HFI assuming previous perfect use (see Section 13.2.1). If CHC has been used in the 7 days prior to EC, the effectiveness of UPA-EC could theoretically be reduced. Consider use of LNG-EC (see Section 10.3).
Combined oral contraceptive pill (monophasic pill containing ethinylestradiol)	Missed pills (if two or more active pills are missed)	EC is indicated if the pills are missed in Week 1 and there has been UPSI or barrier failure during the pill-free interval or Week 1. If the pill-free interval is extended (this includes missing pills in Week 1), a Cu-IUD can be offered up to 13 days after the start of the HFI assuming previous perfect use (see Section 13.2.1). If COC has been taken in the 7 days prior to EC, the effectiveness of UPA-EC could theoretically be reduced. Consider use of LNG-EC (see Section 10.3).

Case 3

The next day Jude (another of Bridget's friends!) attends clinic. She is taking the COCP, Femodene. She started it 1 year ago after surgery for endometriosis. She is really happy with it as a contraceptive as it has improved her acne as well as most of her symptoms from her endometriosis.

She is however getting headaches (not migraines), low mood and a heavy withdrawal bleed in her hormone free interval (HFI).

She is wondering if there is anything that can be done to help these symptoms.

She has heard that she may be able to miss the hormone free interval.

She is wondering if this is safe.

What can you advise Jude?

Facilitator Notes:

No medical indication for HFI or withdrawal bleeds.

Bleed may be inconvenient or painful.

Some women experience symptoms in the HFI due to the fall in hormone levels or the bleeding – these may include headaches, low mood / mood changes, migraine etc. Some medical conditions may be precipitated such as epilepsy in the HFI. In some patient's herpes, thrush or BV may be triggered in the HFI / by bleeding.

Bleed doesn't confirm not pregnant

HFI associated with reduced ovarian suppression – risky time to miss pills.

Shortening the HFI or reducing the frequency of the HFI may help.

This can be done by using tailored CHC regimens e.g.

Shorten HFI

Or

Reduce frequency of HFI, e.g. tricycling (with shortened HFI)

Or

Abolish HFI completely

Or

Flexible extended regimen = take COCP for a minimum of 21 days. If no bleeding carry on taking pill. After 3-4 days of continuous BTB take a 4 day break (HFI). Then take a minimum of 21 days COCP. If no bleeding carry on taking pill. After 3-4 days of continuous BTB take a 4 day break (HFI).

Regimens which involve taking pill in an extended regimen only suitable for monophasic pills – i.e. same dose of hormone throughout.

Play video from CHC webinar if possible.

Annual dose of EE in a 20 mcg EE COCP taken continuously is < annual dose of EE in a 30 mcg EE COCP if taken in conventional 21/7 regimen.

One RCT showed that bleeding control better with 20 mcg EE COCP vs a 30 mcg EE COCP when taken continuously.

Lower dose of EE may minimise cardiovascular risk – limited evidence.

Key messages

No medical indication for a HFI or withdrawal bleed

Endometrium remains thin in continuous regimens – no need to have a bleed every 3 months

Confusion has occurred with clinicians worrying that a women should have a bleed every 3 months – this advice stands for women with PCOS who are oligoamenorrhoeic or amenorrhoeic who because of unopposed circulating oestrogen have an increased risk of endometrial hyperplasia and carcinoma. These women do need to have a bleed induced every 3 months if they are not using hormonal contraception.

Continuous use of CHC resulting in no bleeding is like women who have no bleeds on PO methods – the endometrium remains thin and there is no medical need to have a regular bleed.

Box 3: Key messages for women considering use of tailored combined hormonal contraception regimens

- The evidence from studies is that combined hormonal contraception (CHC) is as safe and at least as effective for contraception if it is taken as an extended or continuous regimen as it is when it is taken in a traditional 21/7 cycle.
- A woman who is using CHC does not need to have a monthly withdrawal bleed to be healthy.
- There is no build-up of menstrual blood inside a woman who uses CHC for an extended time without a break; extended CHC use keeps the lining of the womb thin.
- Withdrawal bleeds during cyclical use of CHC have been reported by women who are pregnant; women should not consider monthly bleeds on CHC to be reassurance that they are not pregnant.
- By using extended or continuous CHC the frequency of withdrawal bleeds and associated symptoms (e.g. headache, mood change) is reduced; this could be useful for women who have heavy or painful bleeding or problematic symptoms associated with the hormone-free interval (HFI).
- The ovaries start to become active during the traditional 7-day HFI. Fewer and/or shorter breaks in CHC use could mean that the risk of pregnancy could ***theoretically*** be lower with extended or continuous regimens than if a 7-day break is taken every month.
- There can be irregular bleeding or spotting in the first few months of CHC use, particularly with extended or continuous regimens; this does not usually mean that there is any medical problem and it generally improves with time.
- The evidence from studies is that using extended or continuous regimens of CHC does not affect the return of a woman's fertility when she stops CHC.

Case 4

The next day you see Juno, a 16 year old patient.

She also wants contraceptive advice.

She has a 3 month old baby girl who she is exclusively breastfeeding.

She has been on the desogestrel only POP for the past 2 months but has found she has had worsening acne.

She asks if she can go back on her old pill, Marvelon – she has found in the past this has really helped with her skin.

She asks is it safe to take this pill while she is breastfeeding.

What can you advise Juno?

UKMEC CHC

Postpartum (in breastfeeding women)		**Evidence**: One systematic review reports that the impact of COC on breastfeeding duration and success is inconsistent. Results are conflicting on whether early initiation of COC affects infant outcomes, but generally find no negative impact on infant outcomes with later initiation of COC. [3]
a) 0 to <6 weeks	4	
b) ≥6 weeks to <6 months (primarily breastfeeding)	2	
c) ≥6 months	1	

Early initiation = before 6 weeks

Later initiation = after 6 weeks

FSRH Postnatal contraception Guideline 2017:

Combined hormonal contraception (CHC)and breasfeeding

Women who are breastfeeding, without additional risk factors for VTE and who wish to use CHC should wait until 6 weeks after childbirth before initiating a CHC method.

A systematic review[65] which included 13 studies demonstrated inconsistent effects of COC on breastfeeding performance (duration of breastfeeding, exclusivity and timing of initiation of supplemental feeding), whether COC initiation occurred before 6 weeks (early initiation) or after 6 weeks (later initiation) following childbirth. The systematic review reported conflicting results on whether early initiation of COC affects infant outcomes (growth, health and development) but generally found no negative impact on infant outcomes with later initiation of COC.

The systematic review[65] reported that when COC was used at or before 6 weeks after childbirth, some studies found less weight gain in infants of COC users compared to non-

users while other studies did not find any effect. No study demonstrated an effect on infant weight gain when COC were started after 6 weeks after childbirth. No study found an effect on other infant health outcomes regardless of time of COC initiation. The body of evidence is limited by older studies using different formulations/doses of estrogen than currently used preparations and poor methodological quality of the studies.

The most recent RCT[66] of fair methodological quality, which randomised women to use either COC (*n*=64) or POP (*n*=63) initiated at 2 weeks after childbirth, found that there was no statistical difference in breastfeeding continuation or supplementation between the two groups 8 weeks after childbirth. There was no statistical difference between the two groups in breastfeeding continuation 6 months after childbirth.

Furthermore, at 8 weeks after childbirth, there were no differences between the two groups in terms of infant growth, as measured by weight, length and head circumference.

Women should be informed about the full range of safe alternative contraceptive methods they can use, particularly during the first 6 weeks after childbirth when the risk of VTE is highest, and that use of CHC methods may exacerbate this risk.