



Royal College of  
Obstetricians and  
Gynaecologists

Setting standards to improve women's health



# Faculty of Sexual & Reproductive Healthcare Clinical Guidance



## Management of Unscheduled Bleeding in Women Using Hormonal Contraception

Clinical Effectiveness Unit  
May 2009

ISSN 1755-103X

Published by the Faculty of Sexual and Reproductive Healthcare  
Registered in England No. 2804213 and Registered Charity No. 1019969

First published in 2009 (Faculty website version updated in September 2009)

Copyright © Faculty of Sexual and Reproductive Healthcare 2009

Permission granted to reproduce for personal and educational use only. Commercial copying, hiring and lending are prohibited.

# FSRH Guidance (May 2009) Management of Unscheduled Bleeding in Women Using Hormonal Contraception

(Date of planned revision 2012)

## Purpose and scope

This Guidance brings together evidence and expert opinion on the management of unscheduled bleeding in women using hormonal contraception [i.e. combined oral contraceptive pill (COC), transdermal patch, progestogen-only pill (POP), injectable, implant or intrauterine system (IUS)]. The term unscheduled bleeding in this Guidance refers to breakthrough bleeding, spotting, prolonged or frequent bleeding (Box 1).<sup>1</sup>

The management of women who present with unscheduled bleeding while using hormonal contraception is challenging. For many women unscheduled bleeding will be due to the contraceptive method itself, and the pattern and duration of bleeding and the likelihood of this settling will vary with the method used (Table 1).<sup>2–13</sup> Women may consider that the contraceptive benefits of a method may outweigh the inconvenience of unscheduled bleeding. After reassurance that there is no serious underlying cause they may be happy to continue use.

The management of women with unscheduled bleeding in the initial months (i.e. 3–6 months) after starting a new method of hormonal contraception may differ from that of women who continue to have unscheduled bleeding in the longer term or who present with a change in bleeding pattern. A clinical history (Box 2) should highlight possible underlying causes (an example being *Chlamydia trachomatis*) and provide a guide to the most appropriate examination, investigation and treatment

### Box 1: Clinically important bleeding patterns in women aged 15–44 years<sup>1</sup>

<b>SCHEDULED BLEEDING</b>	Menstruation or regular withdrawal bleeding with combined hormonal contraception (requiring sanitary protection) <sup>1</sup>
<b>UNSCHEDULED BLEEDING</b>	
<b>Frequent bleeding</b>	More than five bleeding episodes <sup>a</sup>
<b>Prolonged bleeding</b>	One or more bleeding episodes lasting 14 days or more <sup>1</sup>
<b>Irregular bleeding</b>	Between three and five episodes with fewer than three bleeding-free intervals of length 14 days or more <sup>1</sup>
<b>Spotting</b>	May not require the use of sanitary protection <sup>b</sup>
<b>Breakthrough bleeding</b>	Unscheduled bleeding in women using hormonal contraception <sup>b</sup>

<sup>a</sup>Bleeding episodes (reference periods) are used to describe patterns of bleeding over time. The first reference period begins on the first day of method use and lasts at least 90 days.

<sup>b</sup>Definitions of spotting and breakthrough bleeding used in this Guidance.

options required. Reassuringly in community populations, endometrial cancer is very rare in women of reproductive age who are using hormonal contraception or who do not have risk factors for endometrial cancer (such as obesity, polycystic ovarian syndrome, tamoxifen use or unopposed estrogen therapy). Cervical cancer is also rare in this population, especially in women who comply with National Cervical Screening Programmes.

A management plan is outlined and can be tailored to the individual woman (Figure 1). Evidence to support the management plan is provided in this Guidance. This management plan is provided as a guide only and can be used to develop a local care pathway taking account of local expertise or ease of referral/access to specialist services and investigations.

Recommendations are provided where evidence exists. Good practice points have been given where no evidence exists but are based on the clinical judgment and opinion of the expert multidisciplinary group developing this Guidance (see Appendix). This Guidance is not intended to serve alone as a standard of medical care, as this should be determined individually based on available clinical information. This Guidance has been systematically developed using the standard methodology outlined in the Appendix to this document.

## Background

During a normal menstrual cycle the endometrium is exposed to circulating sex steroids. It is the sequential exposure of the endometrium to the natural steroids, estradiol and progesterone, that leads to the characteristic histological features.<sup>14</sup>

Estradiol exposure during the follicular phase is responsible for endometrial proliferation. Exposure to progesterone in the luteal phase results in secretory differentiation. Progesterone is anti-estrogenic and inhibits endometrial growth and glandular differentiation. It is the withdrawal of estrogen and progesterone, in the absence of pregnancy, that triggers the onset of menstrual bleeding.<sup>15</sup>

Exogenous administration of sex steroids, in the form of hormonal contraception, will dramatically influence endometrial histology. The endometrial response to hormonal contraception will reflect circulating sex hormone concentrations plus the dose and formulation of steroid delivery, the route of delivery of the steroid, and the timing and duration of administration.<sup>15,16</sup>

The exact mechanisms of unscheduled bleeding associated with hormonal contraception have yet to be explained. The evidence to date implicates superficial blood vessel fragility within the endometrium as a

**Table 1** Expected bleeding patterns after commencing hormonal contraception and in the longer term<sup>2–13, 20</sup>

Contraceptive method	Bleeding patterns in women in the first 3 months	Bleeding patterns in women in the longer term
<b>COMBINED HORMONAL CONTRACEPTION</b> (pill, patch or ring)	Up to 20% of combined oral contraception users have irregular bleeding. No significant differences between pill or patch use. <sup>2–4</sup>	Bleeding usually settles. <sup>19</sup> Ovarian activity is effectively suppressed.
<b>PROGESTOGEN-ONLY CONTRACEPTION</b> Progestogen-only pill	One-third of women have a change in bleeding and 1 in 10 have frequent bleeding. <sup>5</sup>	Bleeding may not settle with time and ovarian activity is incompletely suppressed. Approximately 10–15% are amenorrhoeic; up to 50% have a regular bleed; 30–40% have irregular bleeding. <sup>10</sup>
Progestogen-only injectable	Bleeding disturbances (spotting, light, heavy or prolonged bleeding) are common. <sup>7,20</sup> Up to 35% are amenorrhoeic at 3 months. <sup>6</sup>	Up to 70% are amenorrhoeic at 1 year. <sup>6</sup>
Progestogen-only implant	Bleeding disturbances are common. <sup>9</sup>	After 6 months use, 30% have infrequent bleeding; 10–20% have prolonged bleeding. <sup>6,12</sup>  Long-acting reversible contraceptive (LARC) guidance suggests: 20% are amenorrhoeic; 50% have infrequent, frequent or prolonged bleeding, which may not settle with time. <sup>6</sup>
Levonorgestrel-releasing intrauterine system	Irregular, light or heavy bleeding is common (in the first 6 months). <sup>20</sup>	65% have amenorrhoea or reduced bleeding at 1 year. <sup>6</sup>  A 90% reduction in menstrual blood loss has been demonstrated over 12 months of use. <sup>11,13</sup>

consistent problematic feature. In addition, local changes in endometrial steroid response, structural integrity, tissue perfusion and local angiogenic factors are likely to contribute.<sup>16</sup> Since there are no established long-term interventions available to manage unscheduled bleeding, a greater understanding of the mechanisms involved is required.

**Bleeding pattern expected with hormonal contraceptives**

Pre-method counselling about expected bleeding patterns may reduce concerns and encourage continued use of the method.<sup>17,18</sup> If bleeding patterns fall outside the expected normal patterns associated with different contraceptive methods at different durations of use (Table 1) then examination, investigation or treatment may be indicated.<sup>2–13,19–21</sup>

**1 Before starting hormonal contraception, women should be advised about the expected bleeding patterns, both initially and in the longer term. (Good Practice Point)**

**Medical eligibility criteria for contraceptive use in women with bleeding**

The *UK Medical Eligibility Criteria for Contraceptive Use* (UKMEC) provides recommendations for the safe use of contraception.<sup>22</sup> Categories for use of hormonal contraception by women with vaginal bleeding are summarised in Table 2.

**Management of women with unscheduled bleeding**

An individual approach should be taken when considering

**Table 2** UK Medical Eligibility Criteria for contraceptive use in women with different patterns of vaginal bleeding<sup>22</sup>

Vaginal bleeding patterns	Combined hormonal contraception	Progestogen-only pill	Progestogen-only injectable	Progestogen-only implant	Levonorgestrel-releasing intrauterine system
Irregular bleeding without heavy bleeding	1	2	2	2	1
Heavy or prolonged bleeding (includes regular or irregular)	1	2	2	2	Initiation 1 Continuation 2
Unexplained vaginal bleeding (suspicious of serious pathology) before evaluation	2	2	3	3	Initiation 4 Continuation 2

UKMEC 1: A condition for which there is *no restriction* for the use of the contraceptive method.  
 UKMEC 2: A condition for which the *advantages of using the method generally outweigh the theoretical or proven risks*.  
 UKMEC 3: A condition where the *theoretical or proven risks usually outweigh the advantages of using the method*.<sup>a</sup>  
 UKMEC 4: A condition that represents *an unacceptable health risk* if the contraceptive method is used.

Initiation: Starting a method of contraception by a woman with a specific medical condition.  
 Continuation: Continuation of a method already being used by a woman who develops a new medical condition.

<sup>a</sup>The provision of a method to a woman with a condition given a UKMEC Category 3 requires expert clinical judgement and/or referral to a specialist contraceptive provider since use of the method is not usually recommended unless other methods are not available or not acceptable.

**Box 2: Points to cover in the clinical history from a woman using hormonal contraception who presents with unscheduled bleeding**

Clinical history taking should include an assessment of the woman's:

- Own concerns
- Current method of contraception and the duration of use<sup>a</sup>
- Use of the current contraceptive method<sup>b</sup>
- Use of medications (including over-the-counter preparations) that may interact with the contraceptive method, or any illness that may affect the absorption of orally administered hormones
- Cervical screening history<sup>c</sup>
- Risk of sexual transmitted infections (i.e. for those aged <25 years, or at any age with a new partner, or more than one partner in the last year)
- Bleeding pattern before starting hormonal contraception since starting and currently
- Any other symptoms suggestive of an underlying cause (e.g. abdominal or pelvic pain, postcoital bleeding, dyspareunia, heavy bleeding)
- The possibility of pregnancy

<sup>a</sup>Progestogen-only methods are more likely to present with unscheduled bleeding than combined hormonal methods, and bleeding with progestogen-only pills is less likely to settle than bleeding with the progestogen-only injectable.

<sup>b</sup>For example, missed pills.

<sup>c</sup>A woman presenting with abnormal bleeding who is participating in a National Cervical Screening Programme does not require a cervical screen unless one is due.

the management of women using hormonal contraception who present with unscheduled bleeding. The decision to examine, investigate and/or treat will depend on a clinical assessment (Box 2).

The clinician making an assessment of women using hormonal contraception with unscheduled bleeding should:

- Take a clinical history
- Exclude sexually transmitted infections (STIs)
- Check the cervical screening history
- Consider the need for a pregnancy test.

A **clinical history** (Box 2) should be taken to identify or exclude some of the possible underlying causes of unscheduled bleeding in women using hormonal contraception. The need for examination and investigation will be determined from the clinical history. Assessment of method compliance is an important part of the clinical history (e.g. pill taking, patch use).

All women using hormonal contraception who have unscheduled bleeding should be assessed to identify the risk of **sexually transmitted infections** (STIs). *Chlamydia trachomatis* is the most common bacterial STI in the UK and although up to 80% of women with *C. trachomatis* are asymptomatic abnormal bleeding may be a presenting symptom.<sup>23–25</sup> Risk factors for STIs include age <25 years, or a new sexual partner, or more than one partner in the last year.<sup>23–25</sup> If deemed at risk for an STI, *C. trachomatis* should be excluded as a minimum. A self-obtained low vaginal swab (SOLVS) can be offered (if available locally) or a first-void urine (FVU) if a speculum examination is not being performed. The decision to test for *Neisseria gonorrhoeae* will depend on the woman's individual sexual risk and the prevalence of this infection locally and if dual testing is available as a routine.

A **cervical screening** test is not a diagnostic test of cancer. The cervical screening history should be checked to ensure that women are participating in a National Cervical Screening Programme. This may have been checked when hormonal contraception was initiated but should be reviewed if a woman presents with unscheduled bleeding. A cervical screen can be taken if due or overdue. No evidence was identified to support cervical screening if not due.<sup>26–28</sup>

A **pregnancy test** should be performed if there has been incorrect method use (such as missed pills, late injection or expelled IUS), drug interactions or illness, which may alter absorption of oral methods. No evidence was identified to suggest that unscheduled bleeding in a woman who has been using her hormonal method *consistently and correctly* is associated with an increased risk of pregnancy.

**2 A clinical history should be taken from women using hormonal contraception with unscheduled bleeding to identify the possibility of an underlying cause. (Grade C)**

**3 Hormonal contraceptive users with unscheduled bleeding who are at risk of STIs (i.e. those aged <25 years old, or who have a new sexual partner, or more than one partner in the last year) should be tested for *C. trachomatis* as a minimum. Testing for *N. gonorrhoeae* will depend on sexual risk and local prevalence. (Good Practice Point)**

**4 Women using hormonal contraception who have unscheduled bleeding who are not participating in a National Cervical Screening Programme should have a cervical screen. (Good Practice Point)**

**5 A pregnancy test is indicated for women using hormonal contraception with unscheduled bleeding if the clinical history identifies the possibility of incorrect method use, drug interactions or illness, which may lead to malabsorption of oral hormones. (Good Practice Point)**

**When may examination NOT be required?**

Unscheduled bleeding in the first 3 months after starting a new hormonal contraceptive method is common (Table 1). Genital examination is not required if after taking a clinical history there are no risk factors for STIs, no concurrent symptoms suggestive of underlying causes, and the woman is participating in a National Cervical Screening Programme (Figure 1). Some women may be happy to continue with the method after this initial assessment but follow-up should be planned as bleeding may persist.

**6 In general, in women attending with unscheduled bleeding using hormonal contraception, examination may not be required if after taking a clinical history there are no risk factors for STIs, no concurrent symptoms suggestive of underlying causes, and the woman is participating in a National Cervical Screening Programme. (Good Practice Point)**

**When is examination required?**

Providing there has been consistent and correct use of hormonal contraception, examination is warranted to visualise the cervix by **speculum** examination (Figure 1):

- For persistent bleeding beyond the first 3 months use
- For new symptoms or a change in bleeding after at least 3 months use of a method
- If the woman has not participated in a National Cervical Screening Programme

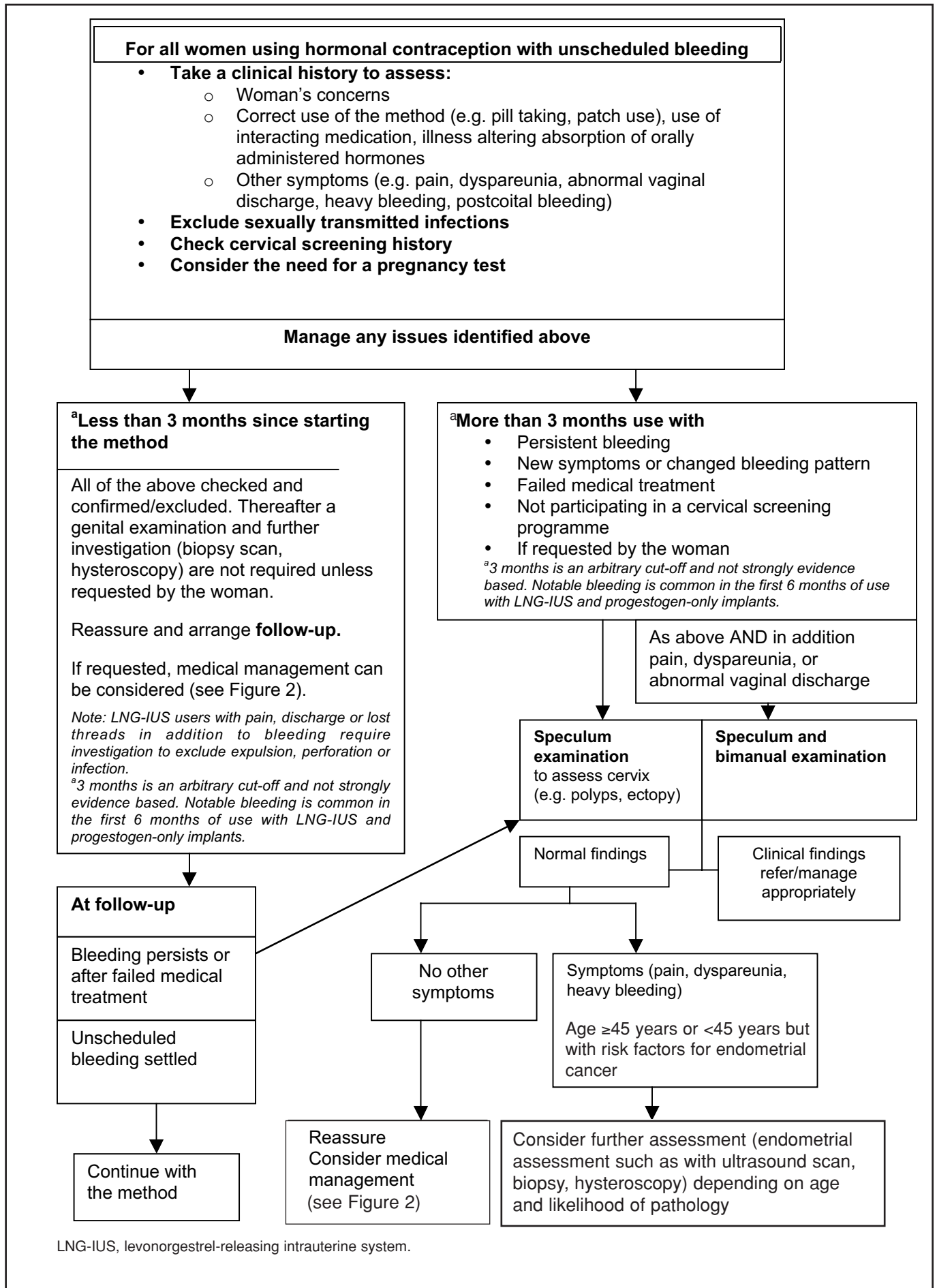
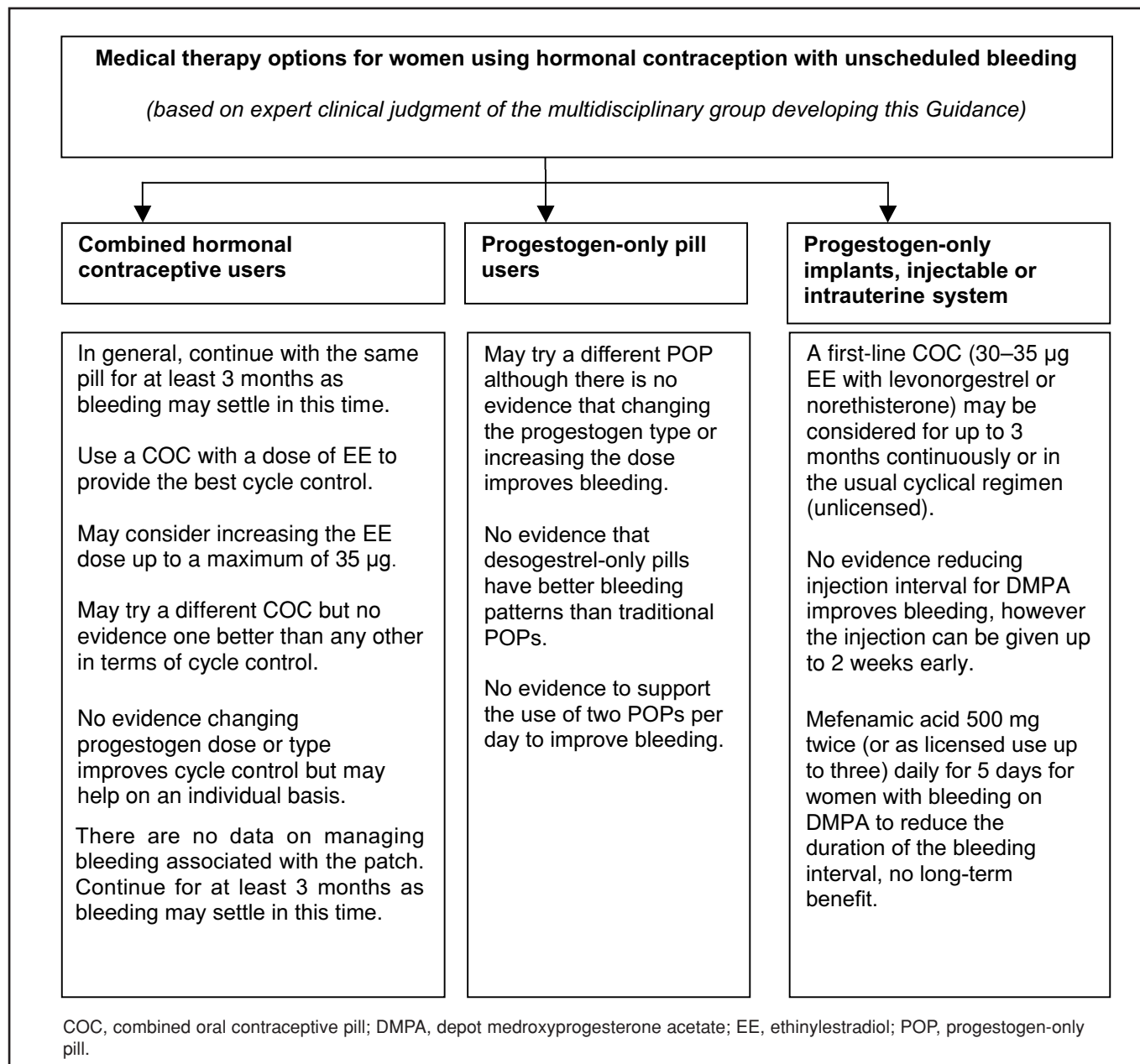


Figure 1 Example of a management plan for a woman using hormonal contraception with unscheduled bleeding



**Figure 2** Medical therapy options for women using hormonal contraception with unscheduled bleeding

- If requested by the woman
- After a failed trial of the limited medical management available (Figure 2)
- If there are other symptoms such as pain, dyspareunia or postcoital bleeding (NB. These symptoms would also warrant **bimanual examination**.)

The 3-month cut-off is given here as a guide only as some methods, in particular the IUS or progestogen-only implant, may commonly cause bleeding after the first 3 months of use. Visualisation of the cervix can identify cervical conditions (such as polyps or ectopy), which may warrant referral for appropriate management. Most cases of cervical cancer are identified by screening. However, visualisation of the cervix may identify the very occasional case of cervical cancer that can present with abnormal vaginal bleeding. Referral for gynaecological examination and an urgent referral to colposcopy is required if cancer is suspected on examination.<sup>26,28</sup>

Guidance from the National Institute for Health and Clinical Excellence (NICE) on the management of women with heavy menstrual bleeding<sup>29</sup> recommends a speculum and bimanual examination if there are additional symptoms (such as intermenstrual or postcoital bleeding, pelvic pain or pressure symptoms suggestive of a structural or histological abnormality). This advice about examinations is appropriate for women with unscheduled bleeding using hormonal contraception.

**7 Providing there has been consistent and correct use of hormonal contraception, a speculum examination should be performed for women using hormonal contraception with unscheduled bleeding if they have: persistent bleeding or a change in bleeding after at least 3 months use; failed medical treatment; if they have not participated in a National Cervical Screening Programme. (Good Practice Point)**

**8** Providing there has been consistent and correct use of hormonal contraception in addition to a speculum examination, a bimanual examination should be performed for women using hormonal contraception with unscheduled bleeding if they have other symptoms (such as pain, dyspareunia or heavy bleeding). (Good Practice Point)

#### When is further investigation (endometrial biopsy, ultrasound scan or hysteroscopy) required?

An **endometrial biopsy** is indicated if endometrial cancer or hyperplasia is suspected. Reassuringly, however, endometrial cancer is rare in women of reproductive age and in addition women using hormonal contraception have a lower risk of endometrial cancer.<sup>30</sup> The commonly used endometrial sampling devices may fail to obtain a sample adequate for pathological diagnosis in up to 10% of women.<sup>31</sup> The use of hormonal contraception (e.g. progestogen-only injectable, which induces endometrial atrophy) may make obtaining an adequate endometrial sample difficult.<sup>32</sup>

There is no guidance available for clinicians on the role for endometrial biopsy in women using hormonal contraception who present with unscheduled bleeding. A NICE Guideline recommends that for women with heavy menstrual bleeding an endometrial biopsy should be performed if there is persistent intermenstrual bleeding, and in women aged  $\geq 45$  years who have treatment failure.<sup>29</sup> This advice may also be useful for women using hormonal contraception with unscheduled bleeding.

Taking account of the lack of direct evidence and the knowledge that endometrial cancer is rare in women of reproductive age, the Clinical Effectiveness Unit (CEU) recommends that an endometrial biopsy may be considered in women aged  $\geq 45$  years. An endometrial biopsy is also recommended in women aged  $< 45$  years with risk factors for endometrial cancer (e.g. obesity, polycystic ovarian syndrome, tamoxifen use or unopposed estrogen therapy) if unscheduled bleeding persists after the first 3 months of starting a contraceptive method or who present with a change in bleeding pattern.

There is no guidance available for clinicians on the role of **transvaginal ultrasound scan** and **hysteroscopy** in women using hormonal contraception who present with unscheduled bleeding. A specific assessment of endometrial thickness is of limited value in premenopausal women but may identify structural abnormalities such as uterine polyps or submucosal fibroids.<sup>29,33</sup>

A NICE Guideline recommends that an assessment of the uterine cavity via transvaginal ultrasound scan or hysteroscopy may be indicated in women with heavy menstrual bleeding who also have signs or symptoms (such as intermenstrual or postcoital bleeding, pelvic pain, pelvic mass) suggestive of a structural abnormality.<sup>29</sup> There is a lack of direct evidence that structural abnormalities (such as uterine polyps or intrauterine fibroids) are the cause of bleeding in women using hormonal contraception with unscheduled bleeding. If, however, these structural abnormalities are suspected a transvaginal scan and/or hysteroscopy may be considered.

**9** In general, an endometrial biopsy should be considered in women aged  $\geq 45$  years (or in women aged  $< 45$  years with risk factors for endometrial cancer (e.g. obesity or polycystic ovarian syndrome) who have *persistent unscheduled bleeding after the first 3 months of starting a method* or who present with a *change in bleeding pattern*. (Good Practice Point)

**10** The role of uterine polyps, fibroids or ovarian cysts as a cause of unscheduled bleeding is limited. Nevertheless, for all women using hormonal contraception with unscheduled bleeding, if such a structural abnormality is suspected a transvaginal ultrasound scan and/or hysteroscopy may be indicated. (Good Practice Point)

#### Treatment options for women with unscheduled bleeding using hormonal contraception

Although numerous research studies have attempted to investigate preventative and therapeutic treatments for women using hormonal contraception with unscheduled bleeding, none are of sufficient quality to guide management in clinical practice usefully.<sup>34</sup> As a result of this lack of evidence, Good Practice Points based on the opinion of the expert group have been given in this section unless otherwise stated.

The *UK Selected Practice Recommendations for Contraceptive Use*<sup>20</sup> (UKSPR) provide recommendations on the management of menstrual abnormalities in women using progestogen-only implants, injectable or IUS. Bleeding with hormonal contraceptives is common in the first few months of use and medical therapy ideally should be delayed until after the first 3 months of use. However, if requested by the woman the limited therapeutic options can be considered in this time.

#### Treatment options for women using combined hormonal contraception

Unscheduled bleeding is less common with combined (estrogen and progestogen) hormonal methods than with progestogen-only methods.<sup>19</sup> Any unscheduled bleeding with the combined oral contraceptive pill (COC) use usually settles with time and therefore changing the COC to another COC in the first 3 months is not generally recommended. Women should use a COC with the lowest dose of ethinylestradiol (EE) to provide good cycle control.<sup>35,36</sup> Cycle control may be better with COCs containing 30–35  $\mu\text{g}$  EE than 20  $\mu\text{g}$  EE.<sup>35</sup>

Data do not support increasing the dose of EE in women already using a 30  $\mu\text{g}$  COC.<sup>37</sup> Nevertheless, increasing the dose of EE to 35  $\mu\text{g}$  may improve bleeding patterns for some women.

Although individual studies suggest bleeding may be better with COCs containing certain progestogens<sup>38–40</sup> this is not evident in systematic reviews.<sup>41</sup>

Using a COC with an extended cycle is safe and well tolerated and indeed the number of days of bleeding is reduced.<sup>42–49</sup> However, there are currently no good data to support the use of a continuous regimen over the licensed cyclical regimes to improve bleeding.<sup>48</sup>

A Cochrane review concluded there was insufficient evidence to recommend the use of a biphasic and triphasic COC to improve bleeding patterns.<sup>40</sup>

Unscheduled bleeding (breakthrough bleeding and



spotting) with the contraceptive patch appeared similar to that for a triphasic COC in a randomised, comparative trial.<sup>50</sup> Unscheduled bleeding was more common in Cycles 1 and 2 with patch use than with COC use.<sup>3</sup>

**11 It is not generally recommended that a combined oral contraceptive pill is changed within the first 3 months of use as bleeding disturbances often settle in this time. (Good Practice Point)**

**12 For women using a combined oral contraceptive pill the lowest dose of ethinylestradiol (EE) to provide good cycle control should be used. However, the dose of EE can be increased to a maximum of 35 µg to provide good cycle control. (Good Practice Point)**

### Treatment options for women using progestogen-only contraception

A Cochrane review investigated preventive and therapeutic treatments of bleeding associated with progestogen-only contraception.<sup>34</sup> No evidence was identified to suggest that bleeding patterns with one progestogen-only method will predict the likely bleeding patterns with another progestogen-only method.

#### Progestogen-only pills

There is a lack of evidence on the effective treatment of bleeding in women using POPs. Studies have investigated the use of an estrogen<sup>51</sup> or an anti-progestogen<sup>52</sup> versus placebo for the treatment of bleeding associated with POP use with little effect. No evidence was identified that suggests one POP is associated with less bleeding than any other (including the desogestrel-only pill). Although bleeding may settle with time, there is no definite time frame in which women can expect bleeding to stop or improve. There is no evidence that bleeding improves with two POPs per day, although this has been used in clinical practice.

#### Progestogen-only injectable contraception

One trial<sup>53</sup> in a Cochrane review<sup>34</sup> evaluated the effect of estrogen on bleeding in women using depot medroxyprogesterone acetate (DMPA). This randomised trial included 278 women using DMPA with irregular bleeding who were randomised to receive either EE (50 µg), estrogen sulphate (2.5 mg) or placebo daily for 14 days. Although this trial of therapeutic treatment was designed to identify both short- and long-term effects, there was a high rate of discontinuation (40% in each group) thus giving a major risk of bias. Only EE was effective in stopping bleeding in the 14 days of treatment [relative risk (RR) 0.26, 95% confidence interval (CI) 0.11–0.60]. In the 3 months following treatment, however, any ongoing beneficial effects of 50 µg EE on bleeding was minimal (RR 0.06, 95% CI 0.00–1.00).

One trial investigated the use of a non-steroidal anti-inflammatory drug (NSAID) (mefenamic acid) for bleeding in women using DMPA.<sup>54</sup> Women had to have at least 8 days bleeding or spotting prior to participating in the trial and to be bleeding on the day of recruitment. This small, randomised, double-blind, placebo-controlled trial found that mefenamic acid (500 mg twice daily for 5 days) was effective in reducing a bleeding episode.<sup>53,54</sup> The usual regimen for mefenamic acid is 500 mg three times daily but there are no studies investigating this dose and its

effect on bleeding. Around 70% of women had stopped bleeding within 7 days of starting mefenamic acid (compared to 40% with placebo;  $p < 0.05$ ). There was no significant difference in the mean bleed-free interval in the longer term (28 days following treatment).

A Cochrane review<sup>34</sup> included trials using estrogen (oral diethylstilbestrol, oral quinesterol or a 17β estradiol transdermal patch) as a preventative treatment for women starting DMPA. The individual trial results were difficult to interpret within the meta-analysis and discontinuation rates were high.

A randomised controlled trial showed that mifepristone (50 mg as a single dose on Day 14 and every 2 weeks for six cycles) reported a significant reduction in breakthrough bleeding compared to women given placebo.<sup>55</sup>

There is no direct evidence on the use of a low-dose (<50 µg) COC to treat unscheduled bleeding in women using progestogen-only injectable contraception. Despite this the UKSPR supports the use of EE (given as a COC) as a *short-term treatment* option in women with light or heavy bleeding with progestogen-only injectable contraception. No recommendation was given regarding the use of an NSAID in the UKSPR<sup>20</sup> and *World Health Organization Selected Practice Recommendations for Contraceptive Use*.<sup>7</sup> More recent evidence of short-term benefit of mefenamic acid has been published.<sup>54</sup>

Based on limited evidence, the CEU recommend that as a *first-line option* a COC may be used by women using progestogen-only injectable contraception with unscheduled bleeding if there are no contraindications to use of estrogen. The COC can be used for up to 3 months while continuing with DMPA (unlicensed use). The COC can be taken in the usual cyclic manner (with a withdrawal bleed) or continuously without a pill-free interval. Based on more recent evidence<sup>54</sup> for women who have a contraindication to COC use then mefenamic acid (500 mg twice or three times daily for 5 days) may be considered to attenuate a bleeding episode but there is no evidence that this approach has an effect on bleeding patterns in the longer term. A small randomised controlled trial<sup>56</sup> suggested that there is some evidence that a Cox-2 inhibitor (valdecoxib) is effective in the treatment of uterine bleeding with DMPA, however the use of Cox-2 inhibitors for this purpose is unlicensed in the UK.

#### Progestogen-only implants

Data relating to management of bleeding problems associated with the etonogestrel implant (Implanon<sup>®</sup>) are limited.<sup>6</sup> Data extrapolated from studies in women using a levonorgestrel implant (Norplant<sup>®</sup>) provide some evidence of a beneficial effect of mefenamic acid or EE (alone or as an oral contraceptive) on bleeding patterns.<sup>57–61</sup> To date there are no data to indicate whether or not the same will be true for the etonogestrel implant (Implanon).

Estrogen generally has been reported to have a beneficial effect in stopping bleeding in women using Norplant and may reduce irregular bleeding during treatment. However, discontinuation due to estrogenic side effects of nausea was common. A combination of oral EE (50 µg) with levonorgestrel (250 µg) taken for 20 consecutive days in Norplant users reduced bleeding during treatment and up to 8 weeks after treatment when compared to placebo.<sup>59</sup> This combined approach significantly reduced continued irregular bleeding during treatment compared to placebo (RR 0.08, 95% CI 0.03–0.24) and reduced unacceptable bleeding (as defined by the number of women having bleed-free intervals of <11 days) after treatment (RR 0.02, 95% CI

0.00–0.29). There is limited evidence that levonorgestrel (0.03 mg) given alone twice daily for 20 days from the eighth consecutive day of bleeding reduced the number of days of bleeding over the following year of Norplant use.<sup>61</sup>

Research suggests that doxycycline and mifepristone may also be beneficial but there is limited evidence to support their use in routine clinical practice.<sup>35,62–64</sup>

For women with light or heavy bleeding with a progestogen-only implant, the use of estrogen as COC or an NSAID is recommended in the UKSPR.<sup>20</sup> Nevertheless, the dosing regime and duration of use are not specified.

#### Levonorgestrel-releasing IUS

No evidence was identified on treatment options for women with unscheduled bleeding with the levonorgestrel-releasing IUS. Good provision of information about expectations of bleeding patterns likely to be experienced is an important part of management.

**13 Bleeding is common in the initial months of progestogen-only method use and may settle without treatment. If treatment may encourage women to continue with the method it may be considered. (Good Practice Point)**

**14 There is no evidence that changing the type and dose of progestogen-only pills will improve bleeding but this may help some individuals. (Good Practice Point)**

**15 For women with unscheduled bleeding using a progestogen-only injectable, implant or IUS who wish to continue with the method and are medically eligible, a COC may be used for up to 3 months (this can be in the usual cyclic manner or continuously without a pill-free interval). (Good Practice Point)**

**16 For women using a progestogen-only injectable contraceptive with unscheduled bleeding, mefenamic acid 500 mg twice daily (or as licensed up to three times daily) for 5 days can reduce the length of a bleeding episode but has little effect on bleeding in the longer term. (Grade B)**

#### References

- Belsey EM, Pinol EP. Menstrual bleeding patterns in untreated women. *Contraception* 1997; **55**: 57–65.
- Zieman M, Guillebaud J, Weisberg E, Shangold GA, Fisher AC, Creasy GW. Contraceptive efficacy and cycle control with the Ortho Evra®/Evra® transdermal system: the analysis of pooled data. *Fertil Steril* 2002; **77**: S13–S18.
- Faculty of Family Planning and Reproductive Healthcare Clinical Effectiveness Unit. New Product Review (September 2003). Norelgestromin/ethinyl oestradiol transdermal contraceptive system (Evra). *J Fam Plann Reprod Health Care* 2004; **30**: 43–45.
- Crosignani PG, Testa G, Vegetti W, Parazzini F. Ovarian activity during regular oral contraceptive use. *Contraception* 1996; **54**: 271–273.
- McCann MF, Potter LS. Progestin-only oral contraception: a comprehensive review. *Contraception* 1994; **50**: S159–S188.
- National Institute for Health and Clinical Excellence (NICE). *Long-Acting Reversible Contraception: The Effective and Appropriate Use of Long-Acting Reversible Contraception*. 2005. <http://www.nice.org.uk/Guidance/CG30> [Accessed 7 January 2009].
- World Health Organization. *Selected Practice Recommendations for Contraceptive Use* (2nd edn). 2005. [http://www.who.int/reproductive-health/publications/spr\\_2/index.html](http://www.who.int/reproductive-health/publications/spr_2/index.html) [Accessed 7 January 2009].
- Aktun H, Moroy P, Cakmak P, Yalcin HR, Mollamahmutoglu L, Danisman N. Depo-Provera: use of a long-acting progestin injectable contraceptive in Turkish women. *Contraception* 2005; **72**: 24–27.
- Funk S, Miller MM, Mishell DR, Archer DF, Poindexter A, Schmidt J, *et al.* Safety and efficacy of Implanon, a single-rod implantable contraceptive containing etonogestrel. *Contraception* 2005; **71**: 319–326.
- Faculty of Sexual and Reproductive Health Care Clinical Effectiveness Unit. FSRH Guidance (November 2008) *Progestogen-only Pills*. 2008. <http://www.ffprhc.org.uk/admin/uploads/CEUGuidanceProgestogenOnlyPill08.pdf> [Accessed 7 January 2009].
- Andersson K, Odland V, Rybo G. Levonorgestrel-releasing and copper-releasing (Nova T) IUDs during five years of use: a randomized comparative trial. *Contraception* 1994; **49**: 56–72.
- Affandi B. An integrated analysis of vaginal bleeding patterns in clinical trials of Implanon. *Contraception* 1998; **58**: 99S–107S.
- Irvine GA, Campbell-Brown MB, Lumsden MA, Heikkilä A, Walker JJ, Cameron IT. Randomised comparative trial of the levonorgestrel intrauterine system and norethisterone for treatment of idiopathic menorrhagia. *Br J Obstet Gynaecol* 1998; **105**: 592–598.
- Noyes RW, Hertig AT, Rock J. Dating the endometrial biopsy. *Am J Obstet Gynecol* 1975; **122**: 262–263.
- Jabbour HN, Kelly RW, Fraser HM, Critchley HOD. Endocrine regulation of menstruation. *Endocr Rev* 2006; **27**: 17–46.
- Smith OP, Critchley HO. Progestogen only contraception and endometrial break through bleeding. *Angiogenesis* 2005; **8**: 117–126.
- Halpern V, Grimes DA, Lopez LM, Gallo MF. Strategies to improve adherence and acceptability of hormonal methods for contraception. *Cochrane Database Syst Rev* 2006; **1**: CD004317.
- Canto De Cetina TE, Canto P, Ordoñez Luna M. Effect of counseling to improve compliance in Mexican women receiving depot-medroxyprogesterone acetate. *Contraception* 2001; **63**: 143–146.
- Rosenberg MJ, Long SC. Oral contraceptives and cycle control: a critical review of the literature. *Adv Contracept* 1992; **8**: 35–45.
- Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. *UK Selected Practice Recommendations for Contraceptive Use*. 2002. <http://www.ffprhc.org.uk/admin/uploads/Final%20UK%20recommendations1.pdf> [Accessed 7 January 2009].
- Westoff C, Heartwell S, Edwards S, Zieman M, Cushman D, Kalmuss D. Oral contraceptives discontinuation: do side effects matter? *Am J Obstet Gynecol* 2007; **74**: 191–192.
- Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. *UK Medical Eligibility Criteria for Contraceptive Use* (UKMEC 2005/2006). 2006. <http://www.ffprhc.org.uk/admin/uploads/UKMEC200506.pdf> [Accessed 7 January 2009].
- Faculty of Family Planning and Reproductive Health Care and British Association of Sexual Health and HIV. The management of women of reproductive age attending non-genitourinary medicine settings with a complaint of vaginal discharge. *J Fam Plann Reprod Health Care* 2006; **32**: 33–42.
- Scottish Intercollegiate Guidelines Network (SIGN). *Management of Genital Chlamydia trachomatis Infection* (SIGN Publication No. 42). 2000. <http://www.sign.ac.uk/guidelines/fulltext/42/index.html> [Accessed 7 January 2009].
- British Association for Sexual Health and HIV (BASHH). *2006 National Guideline for the Management of Genital Tract Infection with Chlamydia Trachomatis*. 2006. <http://www.bashh.org/documents/61/61.pdf> [Accessed 7 January 2009].
- Scottish Intercollegiate Guidelines Network (SIGN). *Management of Cervical Cancer: A National Clinical Guideline* (SIGN Publication No. 99). 2008. <http://www.sign.ac.uk/pdf/sign99.pdf> [Accessed 7 January 2009].
- Shapley M, Jordon J, Croft PR. A systematic review of postcoital bleeding and cervical cancer. *Br J Gen Pract* 2006; **56**: 453–460.
- NHS Cervical Screening Programme (NHSCSP). *Colposcopy and Programme Management: Guidelines for the NHS Cervical Screening Programme* (NHSCSP Publication 20). 2004. <http://www.cancerscreening.nhs.uk/cervical/publications/nhscsp20.pdf> [Accessed 7 January 2009].
- National Institute for Health and Clinical Excellence (NICE). *Heavy Menstrual Bleeding* (NICE Clinical Guideline 44). 2007. <http://www.nice.org.uk/nicemedia/pdf/CG44NICEGuideline.pdf> [Accessed 7 January 2009].
- Scottish Intercollegiate Guidelines Network (SIGN). *Investigation of Post-Menopausal Bleeding* (Section 2: Risk of Endometrial Cancer) (SIGN Publication No. 61). 2002.

- <http://www.sign.ac.uk/guidelines/fulltext/61/index.html> [Accessed 7 January 2009].
- 31 Gordon S, Westgate J. The incidence of failed pipelle sampling in a general outpatient clinic. *Aust N Z Obstet Gynaecol* 1999; **39**: 115–118.
  - 32 Sereepapong W, Chotnopparatpattara P, Taneepanichskul S, Markham R, Russell P, Fraser IS. Endometrial progesterone and estrogen receptors and bleeding disturbances in depot medroxyprogesterone acetate users. *Hum Reprod* 2004; **19**: 547–552.
  - 33 Critchley HOD, Warner P, Lee AJ, Brechin S, Guise J, Graham B. Evaluation of abnormal uterine bleeding: comparison of three outpatient procedures within cohorts defined by age and menopausal status. *Health Technol Assess* 2004; **8**(34): iii–iv, 1–139.
  - 34 Abdel-Aleem H, d’Arcangues C, Vogelsong K, Gulmezoglu AM. Treatment of vaginal bleeding irregularities induced by progestin only contraceptives. *Cochrane Database Syst Rev* 2007; **4**: CD003449.
  - 35 Gallo MF, Nanda K, Grimes D, Schulz KF. Twenty micrograms vs. >20 µg estrogen oral contraceptives for contraception: systematic review of randomized controlled trials. *Contraception* 2005; **71**: 162–169.
  - 36 Akerlund M, Rode A, Westergaard J. Comparative profiles of reliability, cycle control and side effects of two oral contraceptive formulations containing 150 micrograms desogestrel and either 30 micrograms or 20 micrograms ethinyl oestradiol. *Br J Obstet Gynaecol* 1993; **100**: 832–888.
  - 37 Edelman A, Koontz SL, Nichols M, Jensen JT. Continuous oral contraceptives: are bleeding patterns dependent on the hormones given? *Obstet Gynaecol* 2006; **107**: 657–665.
  - 38 Rosenberg MJ, Waugh MS, Higgins JE. The effect of desogestrel, gestodene, and other factors on spotting and bleeding. *Contraception* 1996; **53**: 85–90.
  - 39 Endrikat J, Hite R, Bannemerschult R, Gerlinger C, Schmidt W. Multicenter, comparative study of cycle control, efficacy and tolerability of two low-dose oral contraceptives containing 20 microgram ethinyl oestradiol/100 microgram levonorgestrel and 20 microgram ethinyl oestradiol/500 microgram norethisterone. *Contraception* 2001; **64**: 3–10.
  - 40 Van Vliet HAAM, Grimes DA, Helmerhorst FM, Schulz KF. Biphasic versus triphasic oral contraceptives for contraception. *Cochrane Database Syst Rev* 2006; **3**: CD003283.
  - 41 Maitra N, Kulier R, Bloemenkamp KW, Helmerhorst FM, Gulmezoglu AM. Progestogens in combined oral contraceptives for contraception. *Cochrane Database Syst Rev* 2004; **3**: CD004861.
  - 42 Anderson FD, Hait H. A multicenter, randomized study of an extended cycle oral contraceptive. *Contraception* 2003; **68**: 89–96.
  - 43 Sulak PJ, Carl J, Gopa Gopalakrishnan I, Coffee A, Kuehl TJ. Outcomes of extended oral contraceptive regimes with a shortened hormone-free interval to manage breakthrough bleeding. *Contraception* 2004; **70**: 281–287.
  - 44 Sulak PJ, Kuehl TJ, Coffee A, Pharm D, Willis J. Prospective analysis of occurrence and management of breakthrough bleeding during an extended oral contraceptive regimen. *Am J Obstet Gynecol* 2006; **195**: 935–941.
  - 45 Archer DF, Jensen JT, Johnson JV, Borisute H, Grubb GS, Constantine GD. Evaluation of a continuous regimen of levonorgestrel/ethinyl estradiol: phase 3 study results. *Contraception* 2006; **74**: 439–445.
  - 46 Miller L, Nottter K. Menstrual reduction with extended use of combination oral contraceptive pills: randomized controlled trial. *Obstet Gynecol* 2001; **98**: 771–778.
  - 47 Kwiecien M, Edelman A, Nichols MD, Jensen JT. Bleeding patterns and patient acceptability of standard or continuous dosing regimens of a low-dose oral contraceptive: a randomized trial. *Contraception* 2003; **67**: 9–13.
  - 48 Miller L, Hughes JP. Continuous combination oral contraceptive pills to eliminate withdrawal bleeding: a randomized trial. *Obstet Gynecol* 2003; **101**: 653–661.
  - 49 Edelman A, Gallo MF, Nichols M, Jensen JT, Schulz KF, Grimes DA. Continuous versus cyclic use of combined oral contraceptives for contraception: systematic Cochrane review of randomized controlled trials. *Hum Reprod* 2006; **21**: 573–578.
  - 50 Audet MC, Moreau M, Koltun WD, Waldbaum AS, Shangold G, Fisher AC, *et al.* Evaluation of contraceptive efficacy and cycle control of a transdermal contraceptive patch vs an oral contraceptive: a randomized controlled trial. *JAMA* 2001; **285**: 2347–2355.
  - 51 Johannisson E, Landgren BM, Diczfalusy E. Endometrial morphology and peripheral steroid levels in women with and without intermenstrual bleeding during contraception with the 300 microgram norethisterone (NET) minipill. *Contraception* 1982; **1**: 13–30.
  - 52 Gemzell-Danielsson K, Gemzell-Danielsson K, Killick SR, Croxatto HB, Bouchard P, Cameron S, *et al.* Improving cycle control in progestogen-only contraceptive pill users by intermittent treatment with a new anti-progestogen. *Hum Reprod* 2002; **2**: 588–593.
  - 53 Said S. Clinical evaluation of the therapeutic effectiveness of ethinyl oestradiol and oestrone sulphate on prolonged bleeding in women using depot medroxyprogesterone acetate for contraception. *Hum Reprod* 1996; **11**: 1–13.
  - 54 Tantiwattanakul P, Taneepanichskul S. Effect of mefenamic acid on controlling irregular uterine bleeding in DMPA users. *Contraception* 2004; **70**: 277–279.
  - 55 Jain JK, Nicosia AF, Nucatola DL, Lu JJ, Kuo LJ, Felix JC. Mifepristone for the prevention of breakthrough bleeding in new starters of depo-medroxyprogesterone acetate. *Steroids* 2003; **68**: 1115–1119.
  - 56 Nathirojanakun P, Taneepanichskul S, Sappakitkumjorn N. Efficacy of a selective Cox-2 inhibitor for controlling irregular uterine bleeding in DMPA use. *Contraception* 2006; **73**: 584–587.
  - 57 Kaewrudee S, Taneepanichskul S, Jaisamrarn U, Reinprayoon D. The effect of mefenamic acid on controlling irregular uterine bleeding secondary to Norplant® use. *Contraception* 1999; **60**: 25–30.
  - 58 Alvarez-Sanchez F, Brache V, Thevenin F, Cochon L, Faundes A. Hormonal treatment for bleeding irregularities in Norplant implant users. *Am J Obstet Gynecol* 1996; **174**: 919–922.
  - 59 Witjaksono J, Lau TM, Affandi B, Rodgers PA. Oestrogen treatment for increased bleeding in Norplant users: preliminary results. *Hum Reprod* 1996; **11**: 109–114.
  - 60 Wu SL. Changes in liver function and three metabolites before and after subdermal implantation with Norplant. *Shengzhi Yu Biyun* 1992; **12**: 74–75.
  - 61 Diaz S, Croxatto H, Pavez M, Belhadj H, Stern J, Sivin I. Clinical assessment of treatments for prolonged bleeding in users of Norplant implants. *Contraception* 1990; **42**: 97–109.
  - 62 Cheng L, Zhu H, Wang A, Ren F, Chen J, Glasier A. Once a month administration of mifepristone improves bleeding patterns in Norplant implant users. *Hum Reprod* 2000; **15**: 1969–1972.
  - 63 Massai MR, Pavez M, Fuentealba B, Croxatto H, d’Arcangues C. Effect of intermittent treatment with mifepristone on bleeding patterns in Norplant implant users. *Contraception* 2004; **70**: 47–57.
  - 64 Weisberg E, Hickey M, Palmer D, O’Connor V, Salamonsen LA, Findlay JK, *et al.* A pilot study to assess the effect of three short-term treatments on frequent and/or prolonged bleeding compared to placebo in women using Implanon. *Hum Reprod* 2006; **21**: 295–302.

## APPENDIX: DEVELOPMENT OF CEU GUIDANCE

This Guidance was developed by the Clinical Effectiveness Unit (CEU): **Dr Susan Brechin** (Unit Director), **Dr Madhuri Thakur** and **Ms Lisa Allerton** (Research Assistants) on behalf of the Faculty of Sexual and Reproductive Healthcare (FSRH) in collaboration with the Royal College of Obstetricians and Gynaecologists (RCOG) with a multidisciplinary group of health professionals comprising: **Dr Sharon Cameron** (Consultant Gynaecologist, Dean Terrace Centre and Royal Infirmary of Edinburgh), **Professor Hilary Critchley** (Professor of Reproductive Medicine, University of Edinburgh), **Dr Mehmet Gazvani** (Consultant Gynaecologist and Subspecialist in Reproductive Medicine and Surgery, Liverpool Women's Hospital/RCOG Guideline and Audit Committee Representative), **Dr Ailsa Gebbie** (Consultant in Community Gynaecology, Edinburgh/Vice-President of the FSRH and FSRH Council Representative), **Dr Anna Graham** [GP, Horfield Health Centre, Bristol/Member of the FSRH Clinical Effectiveness Committee (CEC)], **Dr Kay McAllister** (Consultant in Sexual and Reproductive Health, The Sandyford Initiative, Glasgow), **Dr Karen Piegsa** (Consultant in Reproductive Health, Forth Park Hospital, Kirkcaldy) and **Dr Mark Shapley** (GP/Research Fellow, ARC National Primary Care Centre, Keele University). In addition, this Guidance document was reviewed by the FSRH CEC and independently peer reviewed by the following international peer reviewers: **Professor Martha Hickey** (Professor of Gynaecology, School of Women's and Infants' Health, University of Western Australia), **Professor Ian Fraser** (Department of Obstetrics and Gynaecology, University of Sydney) and **Professor Margaret Rees** (Consultant in Medical Gynaecology and Reader in Reproductive Medicine, University of Oxford). Feedback was also received from **Dr Maggie Cruickshank** (Senior Lecturer in Gynaecology Oncology, Aberdeen Royal Infirmary/Representative for the British Society for Colposcopy and Cervical Pathology). Written feedback was received from **Mr Sean Duffy** (Consultant Gynaecologist, Department of Obstetrics and Gynaecology, St James' University Hospital, Leeds), **Dr Christina Fey** (FSRH CEC), **Dr Eva Jungmann** (Consultant Physician in GUM/HIV, London), **Professor Mary Ann Lumsden** (Head of Section, Division of Development Medicine, Glasgow Royal Infirmary), **Dr James McVicker** (Clinical Director, Abacus Clinics for Sexual and Reproductive Health Care, Liverpool), **Ms Shelley Mehigan** (Nurse Specialist, FSRH CEC/The Garden Clinic, Sexual Health Services, Upton Hospital, Slough), **Mrs Lynn Hearton** (fpa user representative), **Dr Sarah Gray** (GP/Primary Care Lead in Women's Health, Cornwall and Isles of Scilly PCT), **Dr Alison Bigrigg** (Director, Sandyford Initiative, Glasgow) and **Dr Janet Wilson** (Associate Specialist in Sexual and Reproductive Health, Belfast Health and Social Care Trust). No competing interests were noted by members of the multidisciplinary group. Administrative support to the CEU team was provided by **Mrs Jane Carmichael**.

**This CEU Guidance was developed in collaboration with the Guidelines Committee and approved by the Standards Board of the RCOG.** The CEU Guidance development process employs standard methodology and makes use of systematic literature review and a multidisciplinary group of professionals. The multidisciplinary group is identified by the CEU for their expertise in the topic area and typically includes clinicians working in family planning, sexual and reproductive health care, general practice, other allied specialities, and user representation. In addition, the aim is to include a representative from the FSRH CEC, the FSRH Education Committee and FSRH Council in the multidisciplinary group. Evidence is identified using a systematic literature review and electronic searches are performed for: MEDLINE (CD Ovid version) (1996–2008); EMBASE (1996–2008); PubMed (1996–2008); The Cochrane Library (to 2008) and the US National Guideline Clearing House. The searches are performed using relevant medical subject headings (MeSH), terms and text words. The Cochrane Library is searched for systematic reviews, meta-analyses and controlled trials relevant to unscheduled bleeding. Previously existing guidelines from the FSRH (formerly the Faculty of Family Planning and Reproductive Health Care), the Royal College of Obstetricians and Gynaecologists (RCOG), the World Health Organization (WHO) and the British Association for Sexual Health and HIV (BASHH), and reference lists of identified publications are also searched. Similar search strategies have been used in the development of other national guidelines. Selected key publications are appraised using standard methodological checklists similar to those used by the National Institute for Health and Clinical Excellence (NICE). All papers are graded according to the Grades of Recommendations Assessment, Development and Evaluation (GRADE) system. Recommendations are graded as in the table below, using a scheme similar to that adopted by the RCOG and other guideline development organisations. The clinical recommendations within this Guidance are based on evidence whenever possible. Summary evidence tables are available on request from the CEU. An outline of the Guideline development process is given in the table on the inside back cover of this Guidance document. Feedback on Guidance documents should be directed to the CEU via e-mail at [ceu.members@ggc.scot.nhs.uk](mailto:ceu.members@ggc.scot.nhs.uk).

Level of evidence	Evidence
Ia	Evidence obtained from meta-analysis of randomised trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well-designed controlled study, without randomisation
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies, correlation studies and case studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Grades of Recommendations	
A	Evidence based on randomised controlled trials
B	Evidence based on other robust experimental or observational studies
C	Evidence is limited but the advice relies on expert opinion and has the endorsement of respected authorities
✓	Good Practice Point where no evidence exists but where best practice is based on the clinical experience of the multidisciplinary group

## SUMMARY POINTS FOR THE MANAGEMENT OF WOMEN USING HORMONAL CONTRACEPTION WHO PRESENT WITH UNSCHEDULED BLEEDING

### PRE-METHOD COUNSELLING

- Before starting hormonal contraception, women should be advised about the expected bleeding patterns both initially and in the longer term.

### INITIAL MANAGEMENT

- A clinical history should be taken from women using hormonal contraception with unscheduled bleeding to identify the possibility of an underlying cause.
- Hormonal contraceptive users with unscheduled bleeding who are at risk of sexually transmitted infections (i.e. those aged <25 years, or who have a new sexual partner, or more than one partner in the last year) should be tested for *Chlamydia trachomatis* as a minimum. Testing for *Neisseria gonorrhoeae* will depend on sexual risk and local prevalence.
- Women using hormonal contraception who have unscheduled bleeding who are not participating in a National Cervical Screening Programme should have a cervical screen.
- A pregnancy test is indicated for women using hormonal contraception with unscheduled bleeding if the clinical history identifies the possibility of incorrect method use, drug interactions or illness, which may lead to malabsorption of oral hormones.

### EXAMINATION AND INVESTIGATION

- Providing there has been consistent and correct use of hormonal contraception a **speculum examination** should be performed for women using hormonal contraception with unscheduled bleeding if they have: persistent bleeding or a change in bleeding after at least 3 months use of a method; or failed medical treatment; or if they have not participated in a National Cervical Screening Programme. In addition, a **bimanual examination** should also be performed for women using hormonal contraception with unscheduled bleeding if they have other symptoms (such as pain, dyspareunia and heavy bleeding).
- In general, an **endometrial biopsy** may be considered in women aged  $\geq 45$  years (or in women aged <45 years with risk factors for endometrial cancer such as obesity, polycystic ovarian syndrome, tamoxifen use or unopposed estrogen therapy) who have *persistent unscheduled bleeding 3 or more months after starting a method or who present with a change in bleeding pattern*.
- The role of structural abnormalities (such as uterine polyps, fibroids or ovarian cysts) as a cause of unscheduled bleeding is limited. Nevertheless, for all women using hormonal contraception with unscheduled bleeding, if such a structural abnormality is suspected a **transvaginal ultrasound scan and/or hysteroscopy** may be indicated.

### THERAPEUTIC MANAGEMENT OPTIONS

- It is not generally recommended to change a combined oral contraceptive pill (COC) in the first 3 months of use as bleeding disturbances often settle in this time. However, a COC with the lowest dose of ethinylestradiol (EE) to provide good cycle control should be used and the dose of EE can be increased to a maximum of 35  $\mu\text{g}$  to provide good cycle control.
- Bleeding is common in the initial months of progestogen-only method use and may settle without treatment. If treatment may encourage women to continue with the method it may be considered.
- There is no evidence that changing the type and dose of progestogen-only pill will improve bleeding but this may help some individuals.
- For women with unscheduled bleeding using a progestogen-only injectable, implant or intrauterine system who wish to continue with the method and are medically eligible, a COC may be used for up to 3 months (this can be in the usual cyclic manner or continuously without a pill-free interval).
- For women using a progestogen-only injectable contraceptive with unscheduled bleeding, mefenamic acid 500 mg twice daily (or licensed up to three times daily) for 5 days can reduce the length of a bleeding episode but has little effect on bleeding in the longer term.

## Discussion Points for Management of Unscheduled Bleeding in Women Using Hormonal Contraception

The following discussion points have been developed by the FSRH Education Committee.

### Discussion Points

- 1 A 23-year-old woman who has been taking the combined pill for several years complains of breakthrough bleeding in the last few months of pill use. What questions are you going to ask her to help ascertain the cause of this recent change of bleeding pattern?
- 2 A 25-year-old woman who has had Implanon® for 1 year complains about the irregular spotting she has always experienced with Implanon. She wishes to control the bleeding while on holiday for her honeymoon. What treatments might be helpful to control the bleeding pattern?
- 3 A 46-year-old woman who has taken the progestogen-only pill for the last 5 years suddenly develops heavy irregular bleeding. What investigations would you need to consider?

## Questions for Management of Unscheduled Bleeding in Women Using Hormonal Contraception

The following questions and answers have been developed by the FSRH Education Committee.

Indicate your answer by ticking the appropriate box for each question

	True	False
1 Women aged <25 years with unscheduled bleeding on the combined pill should have a high vaginal swab performed to exclude <i>Chlamydia trachomatis</i> .	<input type="checkbox"/>	<input type="checkbox"/>
2 It is mandatory to perform a cervical smear in the presence of unscheduled bleeding with Implanon®.	<input type="checkbox"/>	<input type="checkbox"/>
3 Three months of a progestogen-only pill can help settle unscheduled bleeding in users of injectable progestogens.	<input type="checkbox"/>	<input type="checkbox"/>
4 There is no evidence that women taking hormonal contraception consistently and correctly have a higher risk of pregnancy if they experience unscheduled bleeding.	<input type="checkbox"/>	<input type="checkbox"/>
5 <i>Neisseria gonorrhoeae</i> is a common cause of unscheduled bleeding with the combined pill in the UK.	<input type="checkbox"/>	<input type="checkbox"/>
6 Abdominal ultrasound is an important tool in the detection of submucous fibroids and endometrial polyps.	<input type="checkbox"/>	<input type="checkbox"/>
7 Mefenamic acid (500 mg twice daily) was helpful in reducing bleeding episodes in women using injectable progestogens during clinical trials.	<input type="checkbox"/>	<input type="checkbox"/>
8 Biphasic and triphasic combined pills are associated with an improved bleeding pattern compared to monophasic pills.	<input type="checkbox"/>	<input type="checkbox"/>
9 The contraceptive patch is less likely to cause unscheduled bleeding than a standard combined pill preparation.	<input type="checkbox"/>	<input type="checkbox"/>
10 A pill containing 50 µg ethinylestradiol should be prescribed if a woman has persistent bleeding on a lower dose preparation and no cause for the bleeding can be found.	<input type="checkbox"/>	<input type="checkbox"/>

Answers

1 False 2 False 3 False 4 True 5 False 6 False 7 True 8 False 9 False 10 False











## STEPS INVOLVED IN THE DEVELOPMENT OF CEU GUIDANCE

STEP	TIME TAKEN
<p>Formulation of <b>key clinical questions</b> by the Clinical Effectiveness Unit (CEU).</p> <p><b>Systematic literature review</b> involving searching electronic, bibliographic databases by CEU researchers.</p> <p><b>Obtaining and reviewing</b> copies of the full papers of all relevant publications identified through the searches.</p> <p><b>Formal, critical appraisal</b> of key papers and development of short evidence tables.</p>	<p>This process must be completed in a maximum of 8 weeks.</p>
<p><b>Draft One Guidance</b> document is written, providing recommendations and good practice points based on the literature review.</p>	<p>The CEU has overall responsibility for writing the Guidance document. The Multidisciplinary Group and other peer reviewers should highlight inconsistencies and errors or where the text is incomprehensible.</p>
<p><b>Multidisciplinary Group Meeting</b> comprising stakeholders and including service user representation, representation from the Faculty of Sexual and Reproductive Healthcare (FSRH) Education Committee and, where possible, representation from the FSRH Clinical Effectiveness Committee (CEC) and FSRH Council.</p>	<p>A one-day meeting held in Glasgow with the Multidisciplinary Group to discuss the Draft One Guidance document.</p>
<p><b>Preparation of Draft Two Guidance document</b> based on discussion at the Multidisciplinary Group.</p>	<p>The Multidisciplinary Group meeting is held at least 2 months before the Guidance deadline to allow time for development of further drafts.</p>
<p><b>Peer Review of Draft Two Guidance document</b> by the Multidisciplinary Group and the FSRH CEC.</p>	
<p>All <b>written feedback on the Draft Two Guidance document</b> is tabulated and the CEU response to these comments outlined.</p>	
<p><b>Draft Three Guidance document</b> is prepared based on written feedback and is sent to the Multidisciplinary Group and the FSRH CEC. In addition, two independent peer reviewers are identified by the CEC to provide feedback at this stage.</p>	<p>Only minor comments can be accepted at this stage.</p>
<p>The <b>Final Guidance document</b> is published by the FSRH.</p>	<p>Proofreading of the Guidance document is then performed by three members of the CEU team independently and comments collated and sent back by the Unit Director. A pdf version of the Guidance is available on the FSRH website.</p>

## COMMENTS AND FEEDBACK ON PUBLISHED GUIDANCE

All comments on published Guidance can be sent directly to the Clinical Effectiveness Unit (CEU) via e-mail ([ceu.members@ggc.scot.nhs.uk](mailto:ceu.members@ggc.scot.nhs.uk)).

You will receive an automated acknowledgment on receipt of your comments. If you do not receive this automated response please contact the CEU by telephone [0141 232 8459/8460] or e-mail ([ceu.members@ggc.scot.nhs.uk](mailto:ceu.members@ggc.scot.nhs.uk)).

The CEU is unable to respond individually to all feedback. However, the CEU will review all comments and provide an anonymised summary of comments and responses which, after review by the Clinical Effectiveness Committee, will be posted on the Faculty website ([www.fsrh.org](http://www.fsrh.org)) at regular intervals.