FACULTY OF FAMILY PLANNING & REPRODUCTIVE HEALTH CARE
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Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit

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Faculty Statement from the CEU on a New Publication: WHO *Selected Practice Recommendations for Contraceptive Use* Update

Missed pills: new recommendations

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SUMMARY

The World Health Organization *Selected Practice Recommendations for Contraceptive Use* (WHOSPR) was first published in 2002[1] and provides evidence-based recommendations on how to use contraception effectively. The WHOSPR was adapted for UK use by the Faculty of Family Planning and Reproductive Heath Care (FFPRHC).[2] The UK version is available on the FFPRHC website (www.ffprhc.org).[3] Extensive field experience with the first edition of the WHOSPR highlighted to the WHO the need for revised recommendations for missed combined oral contraceptive pills (COCs). The WHOSPR was updated in 2004 and revised guidance on missed pills published.[4] This guidance is now available on the WHO website (www.who.int/reproductive-health).

The FFPRHC endorses the new recommendations from the WHO on missed COCs for the following reasons:

- There is new evidence on which to base guidance.
- The WHOSPR follows a published and rigorous process for assessing the available evidence.[4]
- The recommendations were developed by an international expert panel, with UK representation.
- Field experience shows a need for simple, harmonised guidance.

This Statement summarises the revised WHOSPR evidence-based 'missed pill rules' in formats that we hope clinicians will find useful. We recognise that different individuals favour different styles for the presentation of information. Thus, both tabular and flow chart styles of summary are provided; these convey the same information but in different ways.

The FFPRHC considers that the following statements may also serve as useful *aides memoir* for the 'missed pill rules':

- Whenever a woman realises that she has missed pills, the essential advice is '*just keep going*'. She should take a pill as soon as possible and then resume her usual pill-taking schedule.
- *Also*, if the missed pills are in *Week 3*, she should *omit the pill-free interval*.
- *Also*, a back-up method (usually condoms) or abstinence should be used for 7 days if the following numbers of pills are missed:
  – '*Two for twenty*' [i.e. if two or more 20 μg ethinylestradiol (EE) pills are missed]
  – '*Three for thirty*' (i.e. if three or more 30–35 μg EE pills are missed)

The fpa (Family Planning Association) has produced a revised COC user information sheet to reflect these changes which is available from April 2005.

Background

The World Health Organization (WHO) convened an Expert Working Group to review the evidence and to develop recommendations. They considered the inconsistent or incorrect use of pills to be a major reason for unintended pregnancy. The WHO asked the systematic review question: "What is the effect on contraceptive effectiveness when pills are missed on different days of the cycle?" Overall, the evidence identified was graded as: Level I, fair, indirect (Table 1).

The following principles underlie the WHO Expert Working Group's recommendations:

- It is important to take an active (hormonal) pill as soon as possible when pills have been missed.
- If pills are missed, the chance that pregnancy will occur depends not only on *how many* pills were missed, but also on *when* those pills were missed. Based on data regarding ovulation, the Expert Working Group determined that missing three or more active (hormonal) pills (two or more for ≤20 μg EE pills) at any time during the cycle warrants additional precautions. The risk of pregnancy is greatest when

Table 1 *Levels of evidence used by the World Health Organization*[5]

Recommendations were based on the following levels and categories of evidence:	
Level I:	Evidence obtained from at least one properly designed randomised controlled trial.
Level II-1:	Evidence obtained from well-designed controlled trials without randomisation.
Level II-2:	Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one centre or research group.
Level II-3:	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.
Level III:	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.
Quality of evidence	
Each study was also given a rating of good, fair, and poor based on grading the internal validity of a study.	
Types of evidence	
Direct:	The evidence was based on data directly addressing the question.
Indirect:	The evidence was extrapolated from other relevant data.

active (hormonal) pills are missed at the beginning or at the end of the active pills, i.e. when the hormone-free interval is extended.

- The evidence for 'missed pill' recommendations is primarily derived from studies of women using 30–35 μg EE pills. The limited evidence on 20 μg EE pills suggests that there may be a higher risk of pregnancy when missing such pills than when missing 30–35 μg pills. Accordingly, the Expert Working Group recommended a more cautious approach when missing ≤20 μg EE pills.
- Field experience from the first edition of the *Selected Practice Recommendations for Contraceptive Use* highlighted the need for simple 'missed pill' recommendations.

Combined oral contraceptives (COCs) reduce gonadotrophins thus inhibiting ovulation.[6] Seven consecutive pills are sufficient to inhibit ovulation. The remaining COCs in a pack maintain anovulation in the vast majority of cycles. The COC also has effects on cervical mucus and the endometrium, which contribute to its contraceptive efficacy. Seven consecutive pills are regularly missed in the pill-free interval without losing contraceptive protection. Follicular activity is evident in the pill-free interval but ovulation does not occur.[6–9] Extending the pill-free interval may reduce efficacy but there is wide interindividual variation.[8]

When pills are missed, the inhibitory effects may be lifted sufficiently for ovulation to occur. Thus, intercourse following missed pills may result in pregnancy.[10,11] Studies have suggested that missed pills are much more common than reported.[12,13] In a study using electronic monitoring of pill-taking, up to 88% of women missed pills on two or more consecutive days and up to 51% of women missed at least three pills per cycle, apparently without jeopardising effectiveness.[12]

The WHO Expert Group and others have identified a number of key unresolved issues:

- How do the number and timing of missed COCs affect the risk of pregnancy, and are there substantial variations among individuals or populations?
- How well do practitioners and COC users understand and follow pill-taking instructions, including use of back-up contraception after missed pills?
- Would shortening the hormone-free interval significantly decrease pregnancy rates?
- Are regimens for missed 30–35 μg EE COCs appropriate for COCs with lower doses of oestrogen, especially with regard to the need for back-up protection?
- How accurately do ultrasound findings, hormonal measurements and evaluation of cervical mucus predict the risk of pregnancy during COC use?
- What are the most effective counselling and other communication strategies for maximising consistent, correct and continued use of COCs?

Table 2 *Advice for women missing combined oral contraceptives containing 30–35 μg ethinylestradiol*

Missed ONE or TWO pills: ● She should take a pill as soon as possible and then continue taking pills daily, one each day.* ● She does not need any additional contraceptive protection.
Missed THREE or more pills: ● She should take a pill as soon as possible and then continue taking pills daily, one each day.* ● She should also use condoms or abstain from sex until she has taken pills for 7 days in a row. ● If she missed the pills in the third week, she should finish the pills in her current pack and start a new pack the next day. She should not have a pill-free interval. If the pill-free interval is avoided in this way, she does not need to use emergency contraception. ● If she missed the pills in the first week (effectively extending the pill-free interval) and had unprotected sex (in Week 1 or in the pill-free interval), she may wish to consider the use of emergency contraception.
** If a woman misses more than one pill, she can take the first missed pill and then either continue taking the rest of the missed pills or discard them to stay on schedule.* **Depending on when she remembers that she missed a pill(s), she may take two pills on the same day (one at the moment of remembering, and the other at the regular time, or even at the same time).*
For Everyday pill regimens: ● If a woman misses any inactive pills, she should discard the missed inactive pills and then continue taking pills daily, one each day.

Table 3 *Advice for women missing combined oral contraceptives containing ≤20 μg ethinylestradiol*

Missed ONE pill: ● She should take a pill as soon as possible and then continue taking pills daily, one each day.* ● She does not need any additional contraceptive protection.
Missed TWO or more pills: ● She should take a pill as soon as possible and then continue taking pills daily, one each day.* ● She should also use condoms or abstain from sex until she has taken pills for 7 days in a row. ● If she missed the pills in the third week, she should finish the pills in her current pack and start a new pack the next day. She should not have a pill-free interval. If the pill-free interval is avoided in this way, she does not need to use emergency contraception. ● If she missed the pills in the first week (effectively extending the pill-free interval) and had unprotected sex (in Week 1 or in the pill-free interval), she may wish to consider the use of emergency contraception.
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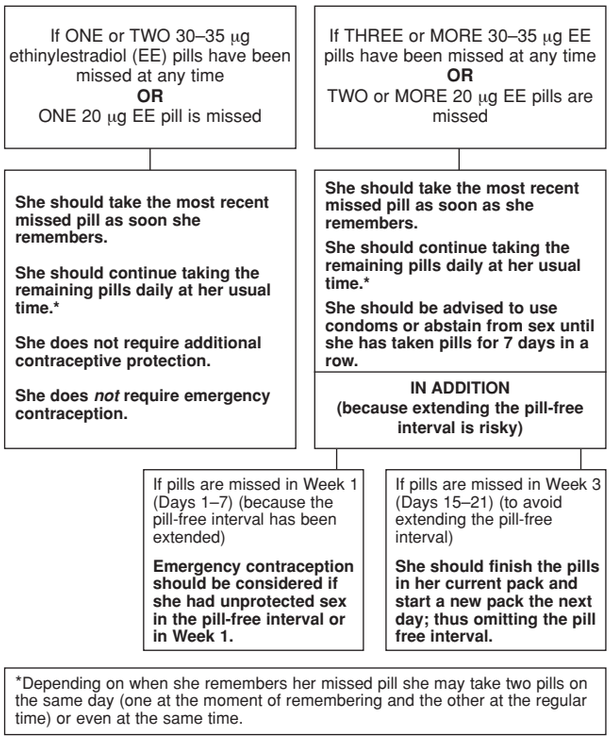

Figure 1 *Advice for women missing combined oral contraceptives (30–35 μg and 20 μg ethinylestradiol formulations)*

This Faculty Statement relates to 21-day pill regimens, and 'missed pills' refers to active, hormone-containing pills. Everyday regimens, which include seven inactive placebo pills, are less often used in UK practice. For women using everyday regimens, the 'missed pill rules' must be modified accordingly.

In applying the 'missed pill rules', clinicians must remember that there comes a point when a woman has missed so many pills that she must be viewed as having stopped taking the pill. The FFPRHC considers that if a woman has missed more than seven consecutive pills, then she has stopped using COC, and the 'missed pill rules' cannot be applied.

Tables 2 and 3 summarise the recommendations from the revised WHOSPR for 30–35 μg and 20 μg pills, respectively. The advice for both 30–35 μg and 20 μg pills is also summarised in a flowchart (Figure 1). Clinicians may use *either* the tables or the flowchart to aid discussions with women, according to individual preference.

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NOTES FOR CONTRIBUTORS

The latest version of the Journal's Notes for Contributors can be found on the Faculty website at **www.ffprhc.org.uk.** The electronic notes are reviewed regularly and updated as required.