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Tailored regimens for combined hormonal contraception (CHC).

The most popular form of contraception in Europe and the US remains CHC (combination of oestrogen and progestogen); this traditionally involves the prescription of 21 days of hormones (21 pills [the most commonly used], or three 7 day patches or one ring for 3 weeks) followed by a 7 day hormone-free interval (HFI) ***(BMJ 2020;368:m200)***. The HFI results in a withdrawal bleed, which mimics a physiological bleed, however **there is no evidence that any bleed is required for safety** (a number of studies have not shown any endometrial thickening or histological abnormalities with continuous CHC use). The UK Faculty of Sexual and Reproductive Healthcare (FSRH) supports the use of "tailored regimens" of CHC in their 2019 updated guidelines; **it highlights that there is no health benefit from the 7 day HFI and that a shorter HFI interval or fewer intervals may improve contraceptive efficacy**. Tailored regimens extend the hormone treatment period for >21 days and reduce the number and frequencies of the HFI; **tailored regimens can only be offered for monophasic preparations that are licensed as a 21/7 regimen** (any placebo pills should be omitted). Women should be advised that tailored regimens are currently outside the manufacturer's licence. The following tailored regimens are supported by the FSRH: **1) Extended use** (often called "tri-cycling") – nine weeks of active treatment (63 pills, 9 patches or 3 rings) followed by a HFI of 4 to 7 days; **2) Flexible extended use** – consecutive pills, rings or patches followed by 4 day HFI taken when desired (contraceptive efficacy is maintained as long as the HFI is preceded by at least 21 days consistent CHC use); **3) Continuous use** – continuous pills, patches or rings without a HFI; and **4) Reduced hormone-free interval** – 4 day HFI instead of 7 days. Tailored regimens allow women to manage their CHC use with the support of their healthcare professional. A Cochrane review found similar satisfaction and continuation rates with women on tailored regimens as those on the traditional regimen. Continuous CHC may be clinically beneficial in patients with heavy menstrual bleeding, dysmenorrhoea, menstrual migraine, acne and endometriosis. Evidence also suggests that tailored regimens are at least as effective (if not more so) from a contraceptive perspective as traditional regimens. The use of CHC is generally safe; there is an increased risk of breast cancer (the risk reduces after 5 to 10 years following cessation of CHC) and there is an increased risk of venous thromboembolism (although the absolute risk is low). A Cochrane review found similar numbers of adverse effects between extended/continuous CHC regimens and traditional regimens, however the trial sizes were inadequate to assess differences in safety. **One of the main challenges with the use of tailored regimens is the management of unscheduled or "breakthrough" bleeding.** Unscheduled bleeding may occur in the first few months of continuous/extended regimens (this may decrease over time in frequency and intensity) and many women also report unscheduled bleeding as "spotting" after several months of continuous CHC use. Treatment of spotting requires a planned short (4 to 7 days) HFI to induce a withdrawal bleed, **followed by restarting CHC which should be for a minimum of 21 days,** before having a further HFI. If the HFI period is >7 days, barrier contraception or abstinence is recommended, until the woman has used CHC continuously for 7 days. FSRH guidelines recommend that the first choice of CHC for any regimen should be ethinyloestradiol ≤30 microgram combined with a progestogen of either levonorgestrel or norethisterone. In addition to discussing tailored regimens at the time of a patient's consultation on contraception, long acting reversible contraception should also be discussed as an alternative contraceptive option, which offers greater contraceptive efficacy than CHC.

[**Editor's note:** The 2019 updated FSRH guideline which discusses tailored regimens as well as other useful guidelines on contraception are available on ***www.fsrh.org***]

Preventable adverse drug events (ADE). ADEs which are defined as unintended and harmful events associated with medications, are a leading cause of unplanned emergency department (ED) visits and hospitalisations. Evidence suggests that between 28 and 80% of ADEs are preventable. A Canadian multi-centre retrospective study combined data from three prospective observational studies which identified patients attending an ED with one or more medication related problems or ADEs ***(Br J Clin Pharm 2020;86:291-302)***. **The aim of the study was to describe the characteristics of preventable ADEs and to highlight factors contributing to them**. A medication chart review was undertaken by 2 independent reviewers to identify ADEs and to highlight ADEs that were considered preventable (a 3rd reviewer adjudicated cases where consensus was not reached). ADEs were considered preventable when there was a lack of adherence to best medical practice (e.g. wrong drug, dose or route); administration of a drug despite a known allergy, a previous adverse drug reaction or a drug-interaction; non-adherence; laboratory monitoring not/inappropriately performed; or medication error. The study found that of the charts of the 3202 patients reviewed with a medication related problem or ADE, **1234 patients were diagnosed with at least one ADE, of which 809 (65.6%) patients were considered to have one or more preventable ADEs.** Those with preventable ADEs were mostly female (56%), median age 71 years and took a median of 8 medications. **Patients with one or more preventable ADEs were more likely to have mental health diagnoses or diabetes, compared to patients with ADEs which were considered non-preventable**. Among preventable ADEs, non-adherence (28.2%), adverse drug reactions (ADRs) (23.8%) and supratherapeutic dosing (13.6%) were most common, while among non-preventable ADEs, ADRs (54.8%), low dose (11.9%) and ineffective drugs (11.7%) were more common. **The most common medications associated with preventable ADEs were warfarin, hydrochlorothiazide, furosemide, insulin and acetylsalicylic acid**, while the most common medication classes associated with preventable ADEs were coumarin derivatives, opiates, atypical antipsychotics, thiazide diuretics and loop diuretics. Multiple factors contributed to preventable ADEs including medication prescribing and monitoring, barriers to adherence, problems with communication and social problems, however **the most frequently identified contributing factor was deemed to be inadequate patient education or instructions**. Common prescribing issues included delays or inadequate clinical reassessment after medication changes.

Prescribing cascades occur when an adverse drug event (ADE) is misinterpreted as a new medical condition, and as a result a second medication (or medical device) is prescribed or a diagnostic test is ordered; this may expose the patient to risk and harm ***(BMJ 2020;368:m261)***. **Patients most at risk of prescribing cascades are older adults, however prescribing cascades can occur in any patient at any time.** Older patients are more likely to have comorbidities, polypharmacy and multiple prescribing physicians, which puts them at risk of potentially inappropriate prescribing (PIP) and ADEs. Prescribing cascades increase the risk of ADEs and have been associated with syncope, traumatic falls, invasive procedures (e.g. pacemaker insertion), drug toxicity in older adults and the prescription of anticholinergic drugs; they also contribute to a patient's pill burden and increased drug spending. The World Health Organisation (WHO) highlighted the prescribing of medicines without harm as an issue and tools such as STOPP/START and Beers criteria have been developed to reduce PIP. The identification of prescribing cascades can reduce the number of unnecessary medications, investigations, consultations and harms, however it may be challenging to differentiate a potential symptom of disease from an ADE, especially in patients with multiple comorbidities who are on polypharmacy. The identification of prescribing cascades in real time is challenging; one way to identify and reverse prescribing cascades is by creating a clinical process map, which is a graphical representation of a patient's medical course, which demonstrates the temporal relationship between the onset of symptoms and the prescribing of one or more drugs or the initiation of medical investigations.

[**Editor's note**: readers are reminded of the HSE's medication safety campaign "Know, Check, Ask", which was launched in 2019 and developed in line with the WHO "Medication Without Harm" initiative. Further information is available on www.safermeds.ie.]

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. ***This newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, Trinity Centre, SJH.*** *Tel: Direct Line (01) 473 0589 or 1850 727 727 Email: nmic@stjames.ie @NationalNmic*