UPDATE ON CONTRACEPTION, Sept 2022

<> "We have not inherited the world from our grandparents - we have borrowed it from our grandchildren" www.ecotimecapsule.com
<> "I've not seen a world environment problem that wouldn't be easier to solve with fewer people, or harder, and ultimately impossible, with more."
Sir David Attenborough 2012 [Patron *Population Matters*]

NB for SRH advice during Covid-19 or similar future pandemics: visit www.fsrh.org/fsrh-and-covid-19-resources-and-information-for-srh/

The WHO's 1-4 scale (see p 14 below) is used here as the basis for discussing eligibility, as at: www.who.int/reproductive-health and in the WHO's essential *Global Handbook for Providers* at www.fphandbook.org. **UKMEC** applies the same 1-4 scale, as agreed by the UK's Faculty of SRH (= FSRH), to numerous (not all) relevant conditions: see www.fsrh.org for this PLUS all the Faculty's excellent Clinical Guidelines. In my writings I term the same scale points **WHO 1 to 4** since there are a few, small, differences from UKMEC, identified in below text by "[JG]" - which I justify from available evidence. Use of some brand names for simplicity does *not* imply endorsement, and the GMC-supported practice of unlicensed use of a licensed product is marked UULP throughout. ***All abbreviations are in the Glossary.***
For users deciding (alone *or in a consultation)* between FP methods, an ideal website is *www.contraceptionchoices.org* *NB: Ultimate responsibility remains with Practitioners, to ensure that advice from any source applies in their client's case.*

UNLICENSED USE, LICENSED PRODUCT (UULP)

This is often termed **'off-label'** or 'Named patient' use [1-2] and is required sometimes for best contraceptive practice. Examples in my judgement, which may or may not be the same as other authorities, appear below as [JG].
The woman should understand that such use, though evidence-based, is not yet licensed. It is best to have a written explanation plus informed verbal consent.

What does UULP require? Acronym is 'EG-RY-PU-RB':
1 Evidence **G**ood [best if *endorsed by a Guidance document*]
2 Responsibility **Y**ours - Pharma Cos. have no interest if it is not in their SPC.
3 Patient* **U**nderstands: though *"...where prescribing unlicensed medicines is supported by authoritative clinical guidance, it may be sufficient to describe in general terms why the medicine is not licensed for the proposed use."* Even so one should usually supply written details: eg 'take 2 pills not 1'
4 Records **B**rilliant - explaining your reasoning for the unlicensed use - with the plan *communicated*, as appropriate
NB For full GMC endorsement of the above, and more, see: *Good practice in prescribing** and managing medicines and devices, paras 103-10.*
www.gmc-uk.org/-/media/documents/prescribing-guidance-updated-english-20210405_pdf-85260533.pdf
NB: Wherever **UULP** appears herein, it indicates *"follow completely the above good practice".*
*Or parent, or carer. **Including online, remotely

COMBINED HORMONAL CONTRACEPTIVES (CHCs)[1,2,3] *The 7-day contraceptive-free interval (CFI) of the COC is too long, should now be consigned to "history".*

The COC was devised in the 1950s. It was a unique contraceptive, the world's first ovarian suppressant. Yet John Rock with Gregory Pincus and the other pioneers supplied women with it along with a unique instruction, for a contraceptive, namely: ***please don't take it* - at all**, for a whole week, 13 times a year! The 7-day pill-free interval (PFI) is, basically and in truth, a contraceptive-free interval[3] (CFI), regularly un-suppressing the suppressed ovary. It was unfortunately based on the calendar and not on data: biochemical and ultrasound data, which did emerge, but 20 years later. The 7-day CFI permits - unsurprisingly - varying degrees of return of ovarian follicular activity. See Figure 1. The top half of this image[2] depicts the daily variation in blood levels of ethinylestradiol and the progestogen after taking COC tablets, and their reduction to zero in the non-taking CFI

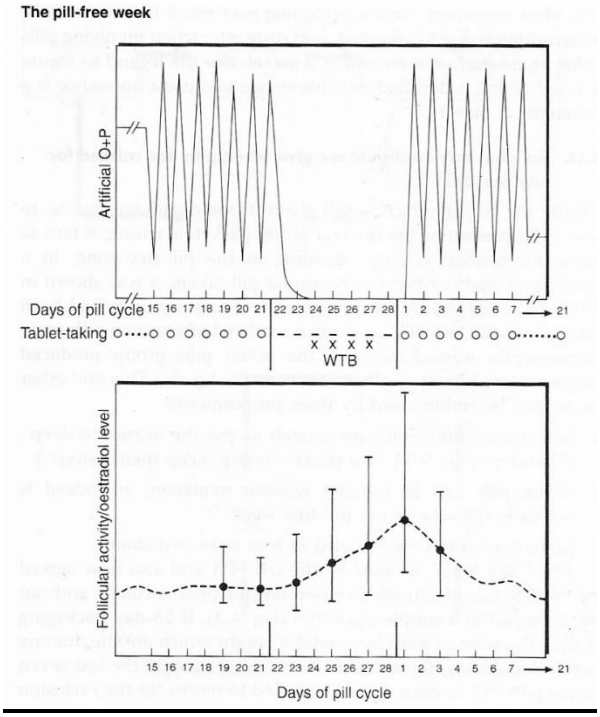
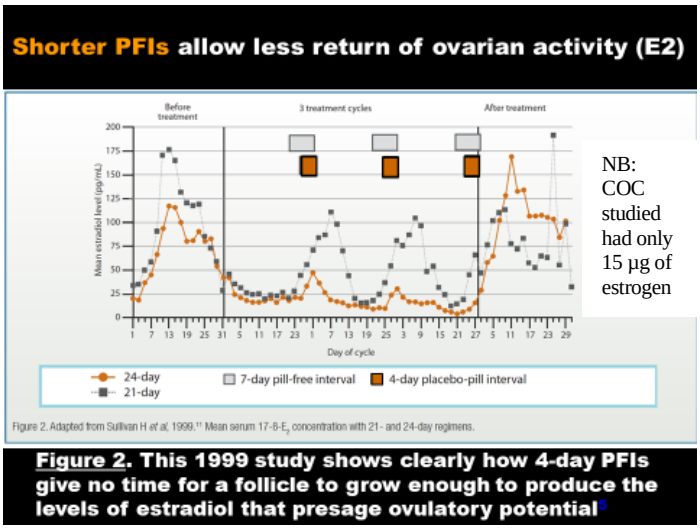


Figure 1

days. The bottom half is based on data from the Margaret Pyke Centre (MPC) in 1978. It shows rising ovarian estradiol [E2] levels in the CFI but can equally represent, in ultrasound studies, the increasing diameter of the largest ovarian follicle: both implying the presence of a maturing preovulatory follicle. In later studies at MPC and elsewhere, individual variation was a feature, with a subgroup, not clinically identifiable though we now know women with high BMIs are over-represented[1], having the greatest increases in E2 levels or follicular diameters. Ultrasound scans showed apparently preovulatory follicles of diameter 10 mm or more on the seventh pill-free day in 23% of 120 pill-takers[4]; in three women the follicle was 16–19 mm in diameter. Such follicles grow by c 2-3 mm per day so can readily reach sizes (mean 21 mm but minimum 16 mm) associated with fertile ovulation, if the 7-day CFI is ever lengthened. However if the CFI is made shorter, see Figure 2[5], ovulation becomes less likely especially when tablets are missed after it: there is more margin for error.



NB: COC studied had only 15 µg of estrogen

Figure 2. This 1999 study shows clearly how 4-day PFIs give no time for a follicle to grow enough to produce the levels of estradiol that presage ovulatory potential[5]

Similarly, the study in Figure 3 showed enhanced ovarian suppression by a 24/4 regimen, but 70% follicular activity and an ovulation rate of 8% if the 7-day CFI was extended to 10 days. Indeed, a *normal* 7 day gap was not very 'safe', since ovulation occurred in 2 out of 99 subjects in the control group if added to the 4+3 days' CFI test group (see 2nd + 3rd bars)[6].

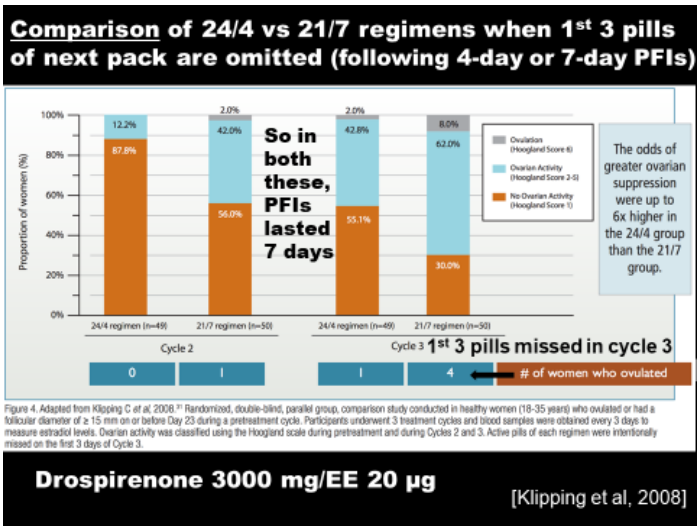


Figure 3

Figures 1-3 account for the failure rates of the traditional 21/7 COC: among 'perfect-users' 3 per 1000 but rising for typical ('ordinary') users up to 90 per 1000 in the first year, an order-of-magnitude worse [Table 1 in ref[1]]. The CFI explains why the method is so 'unforgiving' even after small dosing errors.

But what about the adjunctive contraceptive effect of the progestogen component of COCs on the cervical mucus? At the end of any 7-day CFI this hoped-for back-up will also be at its lowest ebb, it being a week since the progestogen was last ingested. However it can impede fertilization in cases where the CFI-caused ovulation occurs later, early in the next pack.

All studies show no important change during the CFI in the majority of women, ie their ovaries remain quiescent. Yet they also clearly identify that significant c 20 % minority[1-4] with pre-ovulatory activity, leading to two clear conclusions:

<> with traditional 21/7 COCs, integral to all pill-teaching should be to explain how crucial it is never to lengthen the CFI, being "the time when your ovary begins to waken up and could be nearly releasing an egg". All users should learn the *mantra*: ***I must never be a late restarter. I must never….***

<> secondly, in future, the **norm** for all COC-taking now should be, surely, with CFIs that are shortened - or absent.

What if there were *no pill-free intervals (CFIs) at all? ie* <u>Option 1,</u> Continuous 365/[0] pills[1,2,3] ideally with <u>≤</u>20 µg EE**.** Missed-pill advice then boils down to one instruction, to return to regular pill-taking. A succession of tablets can be missed with less ovulation risk than we prescribers have been routinely causing 13 times a year by the advice to "un-suppress" the ovaries for 7 days! Moreover, in the studies since 2003,[7,8,9] cyclical symptoms (namely those not-necessary *scheduled* bleeding days themselves, CFI-linked headaches and the PMS that some COC-users report) are all reduced. Edelman et al[9] in an RCT of LNG versus NET formulations found that sustained use of a pill equivalent to UK's Loestrin 20 led to amenorrhoea *more* often than the EE 30 µg pills tested[8]. Sadly that pill was discontinued in 2020. We await similar RCTs on other 20 µg products: meanwhile they and all the 30 µg EE brands areceptably 'low-dose' for starting shortened-CFI regimens.

Are there disadvantages or risks, if no CFIs?

We await epidemiology, but risks should be low, *given that:*

<> there is no evidence that either the CFIs or 'pill-periods' themselves have any health advantages and

<> 365 days of any 20*µg* EE pill supplies *less* dose [7300 *µg*] of EE than the 8190 µg a year by 21/7 regimens using 30 µg pills. (The 365/[0] regimen lacks that plus point if 30 µg pills are used [10,950 µg EE/year], but evidence does not imply this increases VTE risk if combined with '2nd gen' LNG or NET[1,2])

<> Moreover, to date, compared with 21/7 use, endometrial, reversibility and metabolic data are all reassuring.[9]

Established or Expected Advantages of Pill-taking 365/[0][2, 9]

(NB: nearly all below apply *also* to **tricycling with 4-day CFIs**)

Compared with current 21/7 regimens we expect:

□ *Greater intrinsic efficacy* (when no errors). Less valuable than:

□ *Improved margin for human errors.* Typical ('ordinary') users can then omit many pills with impunity, even that established but unknown subgroup whose ovaries escape COC-suppression fastest. Contrast, currently with 21/7 regimens, only one missed pill is judged 'safe', for fear of lengthening one of the 13 ritual contraceptive-free intervals each year. ***So:***

□ *Greater efficacy in typical use* (significantly so in one study[9], an RCT, albeit with COCs taken vaginally), and overall, *and:*

□ *Rules for missed pills are simple:* 'If up to 4 tablets are missed, provided you have taken at least 7 in a row, return to pill-taking. That's all. If it's 5 or more that you missed, to be extra safe use extra precautions for 7 days.

□ EC for omitted COCs becomes a thing of the past. Usefully, if UPA used, also avoids the added complexity of the advice on return to COC-taking [see p 5]

□ *Lowest-dose COCs are generally (not always) usable,* and so:

□ *Potential as yet unproven for fewer systemic SEs, major or minor*

□ *Fewer total days of bleeding per year, though with the downside of reduced predictability***.** Vaginal bleeding (whether scheduled or unscheduled) having no known health benefits, this is appreciated by many (not all) women. Compare this menstrual protection advantage with the 21/7 regimen, with its *'inevitable' 13 scheduled bleeds* each of say 3-4 days duration. Hence:

□ *More days likely to be available for sex*, and, potentially:

□ *Higher haemoglobin levels.*

□ *Reduced cyclical symptoms* for many, with *less:* –

- *headaches and migraine attacks*[9], which so commonly occur in the pill-free interval
- *menstrual pain*[9], a problem for some in their pill-withdrawal bleeds.
- *premenstrual syndrome-like symptoms*, which are often replicated on COCs when given 21/7
- *epilepsy seizures* (↓ frequency as hormone levels steady).

□ Expected *maintenance of known non-contraceptive benefits of COCs* [this requires epidemiological confirmation]: namely for eg the reduced risk of cancers of colon/ rectum, ovary & endometrium (re the latter, in several continuous-use studies by ultrasound and biopsy hyperplasia was NOT demonstrated[9]). Probably also:

□ *Improved symptoms of endometriosis* (likely because of fewer annual days of bleeding, into any ectopic endometrium).

□ *Maintained reversibility:* in one study of 365/[0] ex-users, they had their first menses or were pregnant by the 90th day![9]

** NB <u>Footnote to box</u>: In the continuous-flexible regimen or 'tailored pill', the woman is advised, in advance, that if she has

unacceptable bleeding/spotting she may take a discretionary 4-day break from pill-taking - on her own "say-so". *Terms apply,* **see below**

Option 2, Tricycling.[1,2,3] This is an extended-use option, suiting women who like to see 'periods'- only less often. JG now advises: *try first a ≤ 30 μg EE COC* taken **63/4** or **84/4**, ie 3 or 4 packs in a row, with *CFIs of 4 days.* [Note: **not** the groundless 7-days of the US products such as Seasonale®]. **These options 1 & 2** are solidly evidence-based and, after all, both are only extensions of "running on packets for holidays" – which is already licensed in most SPCs. Fortunately, any COC-taker may choose either 1 or 2, even now, on a UULP basis[3]. She will need warning that unscheduled bleeds and spotting are probable – esp. in early weeks. She is advised: *"If your bleeding is unacceptable, to you, and has not settled after at least 21 pills in a row since you first started the pill, or after waiting at least 3 weeks since any earlier break: simply* ***stop taking tablets for just 4 days****".* Unless there have been other pill omissions (planned or unplanned) in the last 7 days, no extra precautions are advised). The pill-break provides a form of 'pharmacological curettage', after which, with resumed pill-taking for sufficient time, an acceptable bleeding pattern often follows. With the user given that option, these tricycling and 'continuous-flexible' regimens have full FSRH support at www.fsrh.org/documents/combined-hormonal-contraception/ : *"Women should be told about tailored regimens and given their choice of regimen based on their preference".* This is *empowering*[10]**.**

The evidence-base that the 7-day CFI is contraceptively insecure is indisputable, and the manufacturers are well aware of these data. Indeed most recently marketed COC products are either packaged for continuous or tricycle use – *or,* since 2000, have placebos providing CFIs of 4 days or less (ie 24/4 packaging). Unfortunately however there has been insufficient pressure on the Pharma companies, from prescribers, or unwantedly-pregnant users, to change their SPCs, PILs and if necessary Pill-packaging for *existing* products. We badly need ALL brands simply to update their PILs, after marketing authorization (which at the Regulatory authorities ought to be 'pushing at an open door') for these regimens with absent and/or short CFIs (max 4 days, perhaps using placebos)[3] - usually with minimal expense plus no change in packaging. Does not the box below support this being ***the new norm?***

In Brief, the 'Pros' of Tricycling 63/4 or 365/[0] *vs* 21/7:

1	**Efficacy** – better margin for error, for typical women
2	**Rules** – simpler ++ if dosing errors, & EC 'never'
3	**Dose** – lowest EE dose available, but any ≤ 30 μg ok
4	**Added benefits** – menstrual: ↓ bleeding days & ↓ pain - non-menstrual: ↓headaches & ↓PMS

(These & other issues are amplified earlier, in box on p 2)

Fortunately, we do not have to wait endlessly for updated and licensed PILs. **Options 1 &2 can be used *now,* IF** the simple GMC-endorsed UULP criteria (P 1 Col 1) are met by the provider. Since 2019 the patient information leaflet (PIL) at www.fpa.org.uk/sites/default/files/the-combined-pill-your-guide.pdf now **makes the "new" CHC regimens seem entirely "official" and a CHOICE for any user, though not stating they are preferable.** This leaflet has legal weight and should be routinely given ***plus*** the licensed package PIL. But, missed-pills advice in both is suboptimal; so for now users must follow the wording in above Box p 2 Col 4, bullet 4. Alternatively, they can visit: www.ecotimecapsule.com/pagecontents/pdfs/contraception/continuousflexibleregimen.pdf for our dedicated explanatory PIL [JG], so ending with 3 sources of info'!

Which is absurd and must change, as I say above!

Emphasize to all that though is indeed a "UULP" situation, see p 1 above, that's OK as it is fully evidence-based and is just 'a small change to *make the COC stronger* and also avoid all routine bleeds'. **NB:** the same arguments, and some studies, support the two *non-oral* CHCs, the patch and ring (p 4 below) being used similarly in extended regimens[1, 3].

What about women who wish to take CHCs more 'normally', preferring to have scheduled withdrawal bleeds? It is my belief [JG] that *such women will be ever fewer in number, once both they and their healthcare providers can achieve a complete* ***change of mindset,*** *therefore ceasing that bizarre monthly ritual of deliberately 'un-suppressing' the CHC-suppressed ovaries!* Many will accept reducing their scheduled bleeds to 4-5 per year by tricycling (Option 2). And there is a **third contraceptively acceptable choice** that is currently usable. This is the 21/4 scheme,[3] but that entails over 14 bleeds per year so the user may well soon prefer to tricycle ie 63/4. A poor **fourth option,** surely, is to continue for another 60+ years with the outdated 21/7 regimen….

VTE risk, and the Place of Newer COCs using Estradiol:

LNG and NET progestogens seem to *reduce* relative VTE risk, for any given EE dose[1,2]. The FSRH's updated Guideline www.fsrh.org/documents/combined-hormonal-contraception estimates the absolute incidence for LNG or NET CHCs as c 500-700 vs in the range 900-1200 per million for DSG, GSD, DSP or CPA. Using rough point estimates of c 600 vs c1000 for the mean rates, this means c 400 extra cases per million users per year, and assuming 1% mortality for VTE, gives (if no other risk factor) 4 per million difference in annual VTE mortality between products using LNG/NET and those *not* using LNG or NET. *This added risk would apply if a pill taker chooses to switch from Microgynon®* to say Marvelon®, Femodene®, Yasmin® or Dianette® *but it is very similar to other risks people are prepared to take (eg on the roads, or in outdoor sporting activities).* The small risk of switching is v acceptable for *a side effect, or for acne control.* Yet it remains sensible to ***start with a ≤ 30*** μg ***LNG*** **or NET product**: the usual UK practice.[1,2]

The new Pills (Qlaira®[11] and Zoely®[12]): would they be even safer? Maybe so, since they use the *natural* estrogen E2, which though still prothrombotic is less potently so than EE. The monthly dose is even slightly *lower* than oral HRT and there is some evidence of reduced impact on clotting (eg lower blood levels of D-dimer than Pills with 30 μg EE). We *await epidemiology that confirms* the hoped-for reduced thrombosis risk. It is biologically plausible and if so [JG] *should E2 supplant EE in all CHCs?!* For now, given their high price, Qlaira and Zoely are arguably the products of choice [JG] only **IF** a woman will not accept an entirely estrogen-free alternative method and:

<> WHO 3 applies to CHCs [see p 15], or she is
<> above age 45 with no risk factors, also
<> as a useful 2nd choice of COC for side effects.

Zoely[12] has minor differences from Qlaira [JG]:[1,2] including a simpler pack and the usual 7-day advice for missed pills. Both give cycle control that is OK (withdrawal bleeds can be light or absent) and, usefully, have *short* CFIs with placebos. More generally, the FSRH agrees that the risk of VTE with any CHC is higher:

<> during the first year of use and

<> when re-starting use after an intake break of 4 or more weeks. This finally destroys that widespread *MYTH, that 'it's good to take a break from COC-taking after x years'!*

Other combined hormonal contraceptives (CHCs)

The skin patch Evra® delivers in 24 hours ethinylestradiol (EE) 33.9 µg with norelgestromin 203 µg and can be seen as *"Cilest via the skin"*. NuvaRing® and SyreniRing® deliver 15 µg EE with 120 µg etonogestrel and so roughly equate to *"Mercilon via vagina"*. Hence all absolute and relative contraindications plus most practical management aspects of those COCs apply to these CHCs[1,13], which some women find easier to remember than daily pills. Moreover absorption problems, vomiting/diarrhoea and non-enzyme-inducing antibiotics have no detectable effect on these CHCs.

However both are marketed in 21/7 regimens, with 7-day CFIs - suboptimally, so for ring best use 365/[0] option below.

EVRA®: PK blood level studies of EE and symptoms suggest this is *estrogen-dominant,* and available epidemiology now suggests an increased risk of VTE compared with 30µg COCs. **Avoid use of Evra at all if body weight is >90 kg.** One-third of the few failures in the trials occurred in the 3% above that weight, which must also mean a high BMI - and the Evra blood level & VTE data just given imply it is not a good choice anyway, if there is a risk factor for VTE.

NUVARING® / SYRENIRING®:

Consistent with COCs, scheduled ring-free intervals should be 4 not 7 days. Rings have enough hormone to last more than 5 weeks (Mulders *Fertil Steril*. 2001 May;75(5):865–70) so a good regimen [JG] is 365/[0] using not 13 but 10 of these high cost rings in a year, but with the usual user option as for COCs of a 4-day break to deal with what (on her own say-so) is unacceptable bleeding. The GMC criteria (UULP) of p 1 must be fully met and the Sexwise/fpa CHC leaflet given (see p 3); but in contrast to Evra® above, this continuous regimen is acceptable here because PK studies show lower blood EE levels than the patch. Indeed even though it uses a '3rd generation' type progestogen, a lower VTE risk than with Evra might be expected: *but not yet established.*

There is expulsion potential during coughing/defaecation: but only 2.3% in 1st 13 cycles, 1.7% of which were early on, during the 1st 3cycles (N=3333)[13]. *After expulsion, users may continue with the same ring after simply washing and reinserting.* Ring absence for up to 3 hours is allowed, after that condoms for 7 days are advised.

In pre-market studies *sexual satisfaction increased or was the same in 91% of women.* With enthusiasm from the provider(s) there was high ring satisfaction even in the presence of what was termed "baseline discomfort with genital touching".

In an RCT, many more ring-users than patch users wished to continue the trial product rather than go back to a COC[13]. Usefully, *less BTB plus spotting each cycle was shown through to one year than with Microgynon*[1,2].

PROGESTOGEN-ONLY PILLS (POPs)[1,2]

Following the above thinking about COCs: *not only* is it likely that the 7-day CFIs cause higher doses of EE to be necessary for efficacy than if they were absent; *but also* further reduction must be possible. So why not go down to zero µg of EE? as in the continuously-taken POPs. Moreover these compare well for safety as they do not raise blood pressure or cause thrombosis.

The DSG POP® has many brands besides Cerazette® and contains desogestrel 75 µg. It has been shown to inhibit ovulation in c 97% of cycles, plus having the usual progestogen-related mucus-block as back-up. Hence 'perfect-use' efficacy is better than any previous POP studied, Pearl Index 0.17 (CI 0-0.9)[1,2]. Such efficacy is credible because of the absent CFI and indeed no POP brand has been shown to be any less effective than 21/7 COCs, in studies with 'perfect' use of each! These facts put this specific option in a very good light and support offering it early/first-line to women wanting an oral contraceptive. What a refreshing change from the past when POPs were seen (outside of lactation, see below) as primarily a second choice, needing - almost - to be 'earned', through side effects with COCs or increasing age!

Furthermore the marketing since 2021 of Hana® and Lovima® as over the counter (OTC) products readily purchased on-line - a strongly evidence-based decision - usefully makes them accessible to teens and other young women who are often embarrassed to approach a health care professional for supplies, leading them to risk using far less reliable methods. See p 12.

The DSG POP is also a good choice if the COC is WHO 4 or 3: eg to cover major or leg surgery; or (unlike other POPs), with a history of a past ectopic.

Unacceptable irregular bleeding limits the acceptability of POPs including the DSG POP especially early in use, usually but NOT always improving. At one year 50 % have oligo-amenorrhoea. If unacceptable bleeding continues and no unrelated cause such as *Chlamydia* is found, taking 2 tablets daily (or maybe better, one bd) is worth a trial [JG]: but there are no studies and it is UULP. Consider a LARCr method….

Moderate obesity: '*no current concerns re lack of efficacy'.* Case reports give a little support (JG) to taking 2 tablets daily IF weight is *above 100 kg* (this also is UULP).

POPs and hepatic enzyme inducer drugs (EIDs): to give two DSG POPs while on EIDs is logical[1,2,26]. JG suggests one tablet bd. This doubling is UULP, not advised by the Pharma companies nor, as yet, by the FSRH.

Missed DSG POP pills, outside of lactation (see below)

A 12-hour 'leeway' in pill-taking is now approved, before extra precautions are advised[2]. Then for *all* POPs (DSG POPs included), FSRH advice is that - preceded by EC if there was any UPSI while there was impairment of the POP-induced mucus block to sperm - these need only be for 48 hours after restarting the POP tablets. Just two days added precautions if a woman is not breast-feeding while POPs alter the mucus is now 'traditional'. However the evidence-base that this is enough time to create sperm-impermeable mucus is not very strong. In JG's view there is a case for continuing the 7-day advice, as is stated in most SPCs for POPs[1,2], which is then also congruent with the advice for missed COCs. This allows the anovulation effect of either method to be restored. (One can still say 'the days most *crucial for condom use* are the first two').

QUICK-START [QS] & BRIDGING[14]

Background: Traditionally, initiation of hormonal and intrauterine methods of contraception has been delayed until the next menstrual period, mainly to avoid inadvertent use during pregnancy. But that risk can be minimized, if a medical method is started at the time the woman is first seen, by a careful sexual & menstrual history. Moreover, acc to FSRH: <> large databases show the birth defect risk from exposure to EE or *non-anti-androgenic* progestogens is 'negligible'.

<> Yet, it should be recorded that she has been *warned to stop promptly if she conceives*, ie *before organogenesis* -which occurs after the time of the 1st missed period. Ceasing then makes fetal damage even less likely, so that if this is ensured the ***provider now, with most methods, really needs to have a good reason NOT to propose quick-starting.***

<> Record also the advice: "100% follow-up to confirm not pregnant " - usually by text, email or phone (Practice Nurse). Should there be doubt, a ≤ 20 mIU/L pregnancy test should cost no more than £1 (from *Poundland*® or similar).

<> The main thing is that starting the new method only at the next period risks an avoidable conception *after* she was seen. WHO after reviewing all relevant data concluded this tradition potentially causes *more* morbidity via conceptions than Quick-starting or Bridging as defined at 1 & 2 below.

<> Less important, the woman is *probably* more likely to initiate the new method when seen, than at the next period.

What, according to FSRH[14] (+ JG adaptations), can make a prescriber 'reasonably sure' of a conception risk small enough to justify quick-starting (QS)?

- 'Believable' abstinence since normal LMP
- Within 5 days of normal LMP
- Within 4 weeks post-partum (not lactating)
- Within 6 months post-partum with full breastfeeding (baby's nutrition entirely from mother) & amenorrhoeic [= LAM, 98% effective]
- Within 5 days of abortion/miscarriage/mole
- 'Believable', consistent use of a reliable contra-ceptive (this may include condoms).

Also: <> after hormonal EC, usually (*details below*);
<> and above age 50 - see the **Note**, p 14 Col 1.

More on quick-starting [as ref [14] but with JG's minimal edits: www.fsrh.org/pdfs/CEUGuidanceQuickStartingContraception.pdf]

If a health professional is '*reasonably sure'* (see Box) that a woman is not pregnant from recent UPSI nor on the way to conceiving (ie an unimplanted blastocyst), 'medical' methods of contraception can be started immediately ie ***'quick-started'***, unless the woman prefers to wait until her next period. Such practice for drugs or devices is usually unlicensed (UULP). The woman *must **also** receive the usual advice when starting around mid-cycle*, about abstinence or condom use for - with most hormonal methods - 7 days. ***NB: See special terms below re quick-starts after EC by UPA!***

Bridging is quick-starting exactly as above, except that the woman initiates a pill (POP or COC), but plans with her FP provider, from the start, for this to be short term and to switch later, usually to a LARC. This is often because:

<> her preferred IUS or SDI is not available that day, or

<> recent UPSI requires a -ve pregnancy test, yet *that will only be capable of eliminating conception in 3 weeks time.*

NB bridging can also help to avoid the logistic nightmare of ensuring, in the real world, that IUS or SDI fittings are only done as advised prior to Day 7!

If pregnancy is later diagnosed and the woman wants to go to term, any quick-started method should be ceased, ideally right after the first missed period and so before organogenesis.

Avoid, generally, these mid-cycle ways of commencing if

<> anti-androgens are used, as in Eloine, Yasmin, Qlaira, Zoely and above all in co-cyprindiol - *risk of feminising a male fetus*[2] (see p 11, Col 2), and if

<> LNG-IUS is used: due to concern re high peri-fetal levels of LNG if conception occurred. Yet Turok used it in EC (p 9 Col 1). *Use caution also with DMPA*, whether given im or sc: because, unlike all other contraceptives, once injected it cannot be discontinued. [However no data proves that DMPA causes birth defects, so quick-starting is acceptable, on a case-by-case basis]. **In above cases, initial bridging by POP or CHC till conception can be confidently excluded is preferable** - even ideal, allowing any-day fitting of the IUS or initiation of DMPA. Copper IUDs may always be started immediately if the criteria for use as emergency contraception (EC) are met, see below: with the great advantage that this also 'bridges' to the next period, with long term use to follow in suitable cases, definitely including nulliparae. More is below, in the IUC section pp 8-10.

A most useful protocol:

Immediate 'quick-starting' (= bridging) with a POP (eg DSG POP) or *non-anti-androgenic* COC can be good practice, after a -ve pregnancy test, even when there *have* been one or many UPSIs after the LMP - or when 'no' LMP exists:

<> eg after a *very overdue DMPA injection, defined by the FSRH as 14 or more weeks since last dose* or

<> during *post partum amenorrhoea or*

<> *overdue for replacement of IUS [well beyond 5 years]*

<> *greatly overdue SDI Nexplanon [even beyond 4 years: FSRH[28] since 2021 allows stat insertion plus 7 days' condom use and 2nd pregnancy test at 21-28 days]*

<> *"lost threads" where expulsion or perforation are not ruled out.* See Box:

The *'Proving not Pregnant Protocol'* - with ongoing UPSI[1,2]

After a negative pregnancy test, **or** not done, and with or without hormonal EC as judged necessary, the woman agrees:

<> to ***bridge*** a chosen anovulant OC (DSG POP or *non-*anti-androgenic COC, see text) - and to take it *well*

<> with added precautions initially (eg condoms x 7 days)

<> plus to have a pregnancy test 3 weeks after last UPSI.

<> If compliance good, a negative result establishes no conception (when first seen and more importantly, now). With confidence, can start any LARC or restart any overdue LARC.

<> IF she possibly took the recent OC course inconsistently: for retest (3 weeks after last sex before new method).

EMERGENCY CONTRACEPTION (EC)[15]

Copper is toxic to sperm and also blocks implantation with rapid onset of the effects. Women deserve to know that immediate insertion of a copper IUD is therefore by an order of

magnitude the most effective EC, **with a failure rate of c 1:1000**[16]. The potent anti-implantation effect makes it **usable - - *in good faith* - for EC up to 5 days after the calculated day of ovulation, based on the shortest likely cycle (from history).** It is effective ++ regardless of UPSI episodes and even if the earliest was >120 hours earlier. This is not only legal in UK law, which since 2002 defines conception as not complete till implantation[17], but in JG's view is also ethical[18]. Therefore, if it appears that EC will be given between fertilization and implantation (an interval not less than 5 days), the only truly effective course - despite the perceived 'hassle' for all concerned - is always Cu IUD insertion[16]. Available in UK private practice since 2017, the intrauterine ball (IUB) or 'Ballerine' might may prove to be useful in nulliparae since it has the thinnest insertion tube (3mm). See also below, pp 9-10.

Hormonal EC. Unlike LNG EC[19], **ellaOne® 30 mg stat** is fully licensed for use until 5 days or120 hours after the earliest UPSI. It contains **ulipristal acetate (UPA),** which is a synthetic selective progesterone receptor modulator with antagonist and partial agonist effects. It is a more potent inhibitor of imminent ovulation than LNG EC (Upostelle® & Levonelle 1500®). In a meta-analysis of 2 studies[20] it **prevented over 50% more conceptions than LNG EC, when given on any day post UPSI -** not just days 4 &5 - **IF** followed by abstinence through till the next menses.
UPA EC is more expensive for the NHS but has been shown to be ***cost effective***, through preventing more conceptions.
Without abstinence the failure rate of both EC methods goes up considerably – 4-fold in the case of UPA EC: an argument at first glance for quick-starting the woman's chosen long-term contraceptive. *However, since Sept 2015, if any progestogen-containing method follows after UPA EC, there is an* ***important new policy,*** *as now explained/…:*

Which hormonal EC to use, why, and how?
1 As a progestogen receptor antagonist, it was expected that all quick-started progestogen-containing contraceptives would have their effectiveness reduced after UPA. However, as the FSRH explains, evidence[21,22] that weakening of such methods that *follow* UPA is NOT shown. But there is more:
2 **UPA EC** nearly always DELAYS rather than inhibiting ovulation. Though LNG EC acts by delay less often, we should have been warning *all* EC-takers before now, *that "after working fine today, there might be a fully fertile egg released during the next week".*
3 These data at 2 seemed to reinforce the argument for immediate-starts routinely after hormonal EC; that is, until a study[22] in 2015 showed that, after UPA, the risk of a subsequent fertile ovulation in the **next 5 days** actually *increases highly significantly with next-day quick-starting of a DSG POP.* Sperm, from UPSI before she was seen, might easily survive in the genital tract till then.
4 The mechanism is, unsurprisingly in fact, that DSG reinitiates the ovarian progesterone receptor signalling that the antagonist UPA had blocked.
5 Pending more data the same must apply to all methods containing DSG or indeed any other progestogen.
Therefore **the FSRH's protocol after UPA EC (only)** is, see opposite:

<> *Do not oppose UPA's anti-progestogenicity by the immediate start of any* progestogen, in ANY POP or COC
<> ie *abstinence/condoms* for 5 days post the UPA and:
<> *Only then start the new progestogen-containing FP method, continuing added precautions for the usual time for starts that are later than cycle Day 7* [= 7 days in JG's view].

6 There's been no change in the evidence that, *provided there is no quick-started hormonal method to weaken UPA even for sex before presentation* - UPA EC is more effective than LNG EC. So, ***in high risk cases*:**
UPA is clearly the 'stronger' EC IF a woman accepts abstaining (ideally) for 5 days. She should continue so after a *'semi'-quick-start of* hormonal FP at 5 days, or use condoms well, for 7 further days or until her next period.
7 ***Otherwise,*** the 'strongest' EC of all is always *EC by Cu*. If that is unacceptable and it is also deemed unlikely she will fully comply with the above instructions for UPA EC: 'apply clinical judgement' as the FSRH says, about using LNG EC, since this method has advantages in that:
<> *it allows next-day quick-start of* ***any*** *hormonal method &*
<> *after missing COC pills that lengthened her* [outdated!] *7-day CFI, it permits an immediate restart.* This may make more sense to her than delaying that for a further 5 days.
8 **The reverse, what if UPA is given *after* a progestogen?** Following earlier progestogen use, to allow for long half-lives there should be 7 days of 'wash-out' before UPA EC.

Other facts about UPA EC:
1 There is at least a 20% incidence of a week's delay in start of the next menses *even when the UPA EC 'works'*- no surprise given its mechanism, but must pre-warn about this…
2 The FSRH now advises this may be used *more than once* per cycle, in good faith, avoiding after possible implantation.
3 Above c 70 kg weight UPA EC was significantly more effective than LNG EC[23]. In 2017 the FSRH advice is to use UPA if above 70 kg, or to double the dose of LNG EC (UULP). [**NB** efficacy reduction relates to *weight* not BMI, as linked to dilution of the EC agent in *total body water*].
Any other indications? The prime mechanism of both LNG EC and UPA EC is to delay or less often prevent ovulation. They do *not* seem reliably to cause implantation-block[15,24] at these doses. For that, always offer a Cu-IUD.
Contraindications (WHO 4) to *either* hormonal EC aside from current pregnancy, in my view [JG] are[2]:
<> known **severe** allergy to any constituent of the pills
<> **acute** porphyria with previous severe attack(s) induced by sex hormones.
Caution (WHO 3) applies *with both hormonal methods*, if the woman is on ***an enzyme-inducer*** (including St John's Wort). **This primarily indicates EC by Cu**; but if that is refused or not feasible the hormonal dose may be doubled (UULP). NB this is JG's view, the FSRH currently (since 2017) only supports this for LNG EC[15].
Lactation: EC should rarely ever be needed, see below, but if so either LNG EC or a Cu IUD is preferable. (If UPA EC is used, the SPC advises expressing breast milk for 7 days. .

POST PARTUM CONTRACEPTION[1,2]

With or without breastfeeding, *every* 'medical' FP method may be 'quick-started' stat in the puerperium - EXCEPT:

<> CHCs - Day 21 is the "sweet spot" taking account of ovulation and VTE risk: unless it is judged that a later start would be safer due to complications in the recent pregnancy.

<> IUCs - 4/52 is usual, if missed the option to fit at LSCS.

POPs produce no added DVT or hypertensive risk. Hence, if a LARC is not quick-started:

An excellent protocol [JG] is that *by default, all new mothers* – with of course easy opt-out – *leave their place of delivery already taking a (desogestrel) POP,* as a bridge till they decide on their definitive method such as a LARC. Or stay on it.

With no breastfeeding, the earliest likely ovulation is on Day 28, hence all hormonal methods (Pills, injections, implants and the LNG-IUS) are effective if started then; or 7 days earlier to provide full contraception without added precautions.

Emergency contraception? For a non-lactating woman with post partum amenorrhoea and continuing UPSIs, offer either LNG EC or UPA EC as appropriate - the latter with the now-advised instructions about the new FP method to follow (see points 9 & 10 in the EC section). After Day 28, use the *'Proving not Pregnant Protocol'* (Box on p 5), a much better bet than the too-often-given advice *'use condoms until your next period'*…. which maybe never comes!

Lactation[1,2]

CHCs should not be used pre-Day 42 since they can suppress lactation and are needlessly strong if LAM applies – see Box.

> **Criteria for contraception by the Lactational amenorrhoea *method* (LAM)**
> <> Amenorrhoea, since the lochia ceased
> <> Full lactation—the baby's *nutrition* is effectively all from its mother, sips of water only allowed
> <> Baby not yet 6 months old
> *If and only if all 3 of these are true, this method is 98% effective to 6 months - and v close to 100% if a daily POP taken also (normal practice).*

LAM is among the *recommended* 'natural' methods[25]. There is much more on all these at the superb URL www.fertilityuk **or** www.fsrh.org/documents/ceuguidancefertilityawarenessmethods/

POPs including DSG POPs: started post partum at Day 21 - or (like Nexplanon below), it could be at any time up to then after the birth - are the **first-choice hormonal method in lactation** and no added precautions are advised. So effective is that combination that EC is very rarely indicated for missed POPs. But because breastfeeding varies in its intensity, if an old-type POP tablet (not the DSG POP) is 3 hours late it is still 'traditional' to advise additional precautions during the next two tablet-taking days. Beware of the loss of POP efficacy as, in due course, diminishing breastfeeding ceases to make up for likely less-than-perfect POP-taking: a possible reason for choosing a DSG POP in lactation. Otherwise consider providing, for longer term use, a CHC or a LARC in advance of weaning.

Nexplanon uses the same hormone as the DSG POP and is similarly usable from day 1 after delivery, with some expectation of acceptable oligo-amenorrhoea to follow - by comparison (for some) with insertion at other times.

IUDs and the LNG-IUS are insertable from 4 weeks; but should be deferred (WHO 4) if there is puerperal sepsis, or in trophoblastic disease with persistent urinary hCG.

Contraception after pregnancies that end well before term, including medical and surgical terminations: for this and more see: www.fsrh.org/standards-and-guidance/documents/contraception-after-pregnancy-guideline-january-2017

LONG-ACTING REVERSIBLE CONTRACEPTIVES[27]

SUB-DERMAL IMPLANT (SDI): Nexplanon®

This is a single 40 mm x 2 mm sub-dermal rod releasing etonogestrel (the active metabolite of desogestrel),[28] and differs from Implanon ONLY by containing some barium, so it is radio-opaque. The FSRH now prefers siting it over the triceps to biceps www.fsrh.org/documents/fsrh-ceu-statement-on-nexplanon-insertion-site-15-january-2020/ but the crucial thing is to avoid the neuro-vascular bundle, in the sulcus between the muscles. If the practitioner is *seated*, the risk of deep insertions is reduced since s/he can see the bevel of the applicator-needle as it proceeds sub-dermally. Use minimum LA so as not to mask the palpation that should always prove successful insertion.

Online-based training is accessed through www.fsrh.org. E-training for clinicians (*nurses or doctors*) must be supplemented by hands-on insertion and removal experience using model arms, followed by supervised live-patient training and then by doing at least 12 insertions/year.

Efficacy: aside from vasectomy, the true failure rate of Nexplanon (c 5:10,000) is unmatched over 3 years, indeed better than most methods till 4 years[28] (UULP). To avoid first-month conceptions *a good routine is to quick-start an anovulant method at counselling and **bridge** until the insertion day*, 'overlapping' with it.[1,2]

Unacceptable bleeding: Unacceptable frequent or prolonged bleeds still affects around a fifth of users at one year. Forewarning with reassurance is crucial. Pre-existing amenorrhoea may help, eg during lactation. See below re a way of *hopefully pre-empting this problem through a policy of preliminary DMPA, long enough to cause amenorrhoea.*

With both **DMPA** *(below) and* **Nexplanon**: first, by using a modified version of JG's **'D-Checklist'** for breakthrough bleeding [see Appendix], eliminate an unrelated cause for the bleeding, such as **D**isease (eg Chlamydia) or **D**rugs (EIDs). Then try (the evidence gets weaker lower down the list here):

1 **Three cycles of EE** via any suitable 20-30 µg COC. This usually controls the bleeding within a week while the tablets are being taken, accompanied by monthly shedding of the woman's spotting-prone endometrium through the 'pharmacological curettage' between packs. Thereafter the woman may obtain (not invariably) what she considers an acceptable bleeding pattern - though she should be pre-warned that it is unlikely to be so good as during the short-term COC. The latter treatment is *repeatable prn* while retaining the Nexplanon; or with DMPA, though there is a useful alternative, namely to give doses every 8-10 weeks.

2 Should the COC be WHO 4, try **mefenamic acid 500 mg twice daily** or naproxen 500 mg bd for 5 days or longer with clinical judgement. There is RCT support for the former[2], for stopping a prolonged bleeding episode.

3 Another possibility which seems to help in some cases but is NOT yet fully evidence-based, is to give **added oral**

progestogen (UULP) eg a daily oral DSG POP tablet or Provera® 10 mg 8-hourly. **Crucially**, NET Primolut N® is *not good* for this (nor for postponing periods): the SPC warns re VTE risk, each 1 mg of NET being metabolised to c 4 µg EE !! Now preferred: use MPA (Provera®) 10 mg 8-hrly.
Always consider, also, the option of switching altogether, to *another contraceptive – maybe Kyleena®, see below.*
Nexplanon and EIDs: The SPC reports that these lower the blood levels of etonogestrel and conceptions have occurred. Therefore avoid the SDI method if long term EID treatment is planned (eg in epilepsy). Women on *short term treatment* with one of these drugs are advised to use a barrier method also and (because reversal of enzyme induction is slow) for 28 days thereafter. During *long-term EID treatment*, MSD (the Pharma) recommends transfer to an unaffected method. Given that ***EID users do very well with DMPA or an IUS or a Cu IUD*** (see below), these are definitely preferred.
Bone density: unlike DMPA (see below), the data do not yet support concern re this in SDI-users: but there is uncertainty.[28]

INJECTABLES

DMPA, given as Depo-Provera® im[30] or Sayana Press® sc.[31]
Normal dose of the former is 150 mg im, every *12 weeks*, though interestingly, and it is well evidence-based, in many countries the usual frequency is 13-weekly, which is the same as, in the UK now, the 104 mg sc dose of **Sayana Press[31].** This DMPA product is almost the same price as 'Depo' and *everything about Depo-Provera also applies to Sayana Press*: except of course *the different instructions for the injection process, explained for both providers and users in a most helpful 7-step animated film on Pfizer's website*
www.sayanaanswers.co.uk/guide-to-self-injection
The subcutaneous route into abdomen or anterior thigh:
<> is advantageous in gross obesity
<> minimises haematoma risk for those on anticoagulants, and
<> has the potential for self-injection (approved in Sept. 2015).
This last makes it more practical to implement for DMPA **the elimination of *routine* follow-up visits,** as indeed is now recommended for most methods. WHO and the FSRH recommend that, instead of these, there is a truly **'Open House' policy** for all healthy, normotensive users of hormonal contraceptives, including injectables all the CHCs, POPs and Nexplanon – and IUCs, see below. **'Open House'** ensures that users who have any concerns about their method are seen promptly, at any time after its initiation, *upon request*.
New users of injectables: The *unique features* should be discussed with new users of both these forms of DMPA, namely: (a) once injected it cannot be removed; (b) it causes delay in return *(but **no** loss)* of fertility; and (c) it is probably capable of causing the weight gain for which it is blamed (not proven for any other hormonal method)[2], a risk focussed in under-18s with BMI > 30. But weight gain is ***not*** certain for every case, the problem can be pre-empted by forewarning and relevant advice! *Forewarn also* about the likely irregular bleeding: if it occurs, unacceptably, for management see at **Nexplanon** above.
Also, when given **subcutaneously** rather than im, *it is crucial to warn that* **skin reactions are not uncommon.** These, including irritation, induration & even indentations from fat atrophy, can be minimised but NOT always prevented by varying injection sites.
Grossly overdue injections with continuing UPSI? See the *'Proving not Pregnant Protocol'* in Box, page 5, with refs 1-2.
Drug interactions? NB: in a DMPA study[32] there was 100% clearance from the blood by the liver, specific to this progestogen. DMPA either as an im or sc depot, is therefore an **excellent choice for women on *enzyme inducer drugs (EIDs)***, since they cannot increase this already 100% clearance. As a consequence both Pfizer and FSRH/UKMEC advise no change in dose or in the usual injection frequency during EID use.
How long to use DMPA? given the ongoing concern about low estrogen reducing bone density, in a minority. If this occurs, there is evidence of reversibility both in younger and older women; but uncertainty persists[1,2]. **In summary**: The protocol introduced in an MHRA circular (2004) requires *"careful re-evaluation of risks and benefits"* every 2 years, comparing with other relevant contraceptive options.
For the few young women with known risk factors for osteoporosis already, DMPA is WHO 4, maybe 3.
Under age 18, due to concern that it may - mostly reversibly - reduce achievement of peak bone mass, UKMEC classifies DMPA as WHO 2; and the UK advice since 2004 is it is fine to use first-line in teens "but **only** after other methods have been discussed" and are unsuitable or unacceptable. DMPA is also WHO 2 above age 45, for obvious reasons. In sum, DMPA is very useful though (now) being seen as a relatively short term method, after which switching to another method is usual. A good choice then can be Nexplanon, which for a user is a bit like DMPA with one's injection 3-yearly rather than 3-monthly... For teens and indeed others, JG's suggested routine policy with implants is to plan to use DMPA first. Oligo-amenorrhoea is established usually well within 1-2 years, aided if needed by giving the injections 8- or 10-weekly (UULP). There is then a good chance (but no certainty) this will be maintained after the Nexplanon is inserted: thus hopefully pre-empting Nexplanon bleeding problems… Moreover the insertion can then be at any time: no fear of an insertion-cycle conception…. Another 'plus' of this policy is the shortish duration of DMPA use, meaning less weight gain concerns.
If the woman wishes to use DMPA for **much longer than 2 years,** it is as always her right to decide to do so, after counselling about the uncertainty. This should be ***with*** continuing 2-yearly reassessment of alternatives ***but without bone scanning or blood tests unless clinically indicated,*** for that woman. NB: Relevantly, being estrogen-free, DMPA is overall objectively *safer* than any CHC as an alternative.
Same problem with long term Nexplanon? Initial data was reassuring re both estradiol levels and bone mineral density. However the 2021 FSRH Guidance is more cautious, stating the evidence "cannot confirm or exclude" this risk[28]. Yet to date there are no such concerns re the DSG POP - nor re the LNG-IUS, whose primary actions are uterine, not at the ovary.

INTRAUTERINE CONTRACEPTION (IUC)

This means IUDs or IUSs or now the IUB (intrauterine ball, new since 2017) - all termed generically IUCs. **Not** '*coils*', a word which some find a tad off-putting! Their efficacy justifies the term 'reversible sterilization.'[1,2, 33-36] See p 10.
Among IUDs *a banded IUD should be the first choice*, given efficacy which is only slightly less than the LNG-IUSs.

The *main* advantage over Cu-wire-only IUDs is *not* just greater efficacy[36] but their durability for more than 10-years *in situ* - because research in the past 50 years has clearly shown that most IUD complications can be (re-) insertion-related. They also reduce in frequency with greater duration of use. The *banded* T-Safe Cu 380A IUD (eg TT 380 Slimline) has been the 'gold standard. However in a 2019 observational study[37], statistically fewer complaints of pain and bleeding with fewer discontinuations were recorded by 1 year among users of the **Mini TT 380 Slimline** (Durbin), regardless of parity. Since this mini-IUD has exactly the same amount of contraceptive Cu as the larger TT 380 Slimline comparator, and hence is usable like it for ≥10 years (UULP), pending more data it should [JG] now be preferred, as *first line for parous as well as nulliparous women.* For other options see below.

NB: *Forget the myth!* Nulliparity is *not* WHO 4 for IUCs!
In mutually monogamous relationships intrauterine methods should be seen as WHO 2, rarely 3, and *suitable for a trial* with (as always) later removal as an option.

***Duration of use*:** UK practice since 1990 is that ANY *copper IUD fitted above age 40* can be used - given declining fertility thereafter - *for the rest of reproductive life*.

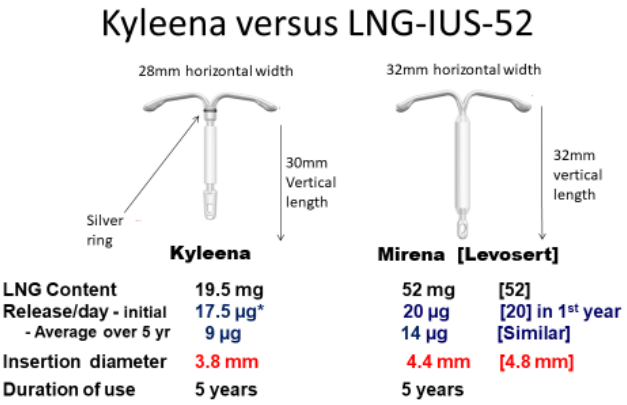
When to use other IUDs? In a RCT the **Nova T380** which has *copper wire but no bands*, was effective but less so than the T-Safe Cu 380A (cumulative failure rate at 3 years 3.6 vs 1.7)[36]. The **UT 380 Short** (Durbin) is Nova T style, with an identical insertion tube, narrower (3.6 mm) than the banded Mini TT 380 (4.75 mm) and licensed for 5 years, but on a shorter stem, useable for cavities down to 6 cm on sounding. So in my view [JG], when there are actual or anticipated technical problems in fitting the Mini TT 380, eg in nulliparae for EC, this is probably the next best choice. New competitors are **VeraCept®** [not marketed] and the **IUB [SCu300B** MIDI**].** The latter's very narrow (3.2 mm) insertion tube makes it of interest, esp for EC, though questions remain to be answered - see: www.fsrh.org/documents/new-product-review-intrauterine-ball-iub-scu300b-midi-february/ The **Flexi-T 300/Cu-Safe T300** is a third narrow-tube option, but licensed for only 3 years.

***NB:** If with any Cu-IUD heavier bleeding or pain are, in fact or in prospect, unacceptable: offer a direct switch to a LNG-IUS.*

LNG-IUS[1,35] Levosert®, Mirena®, Kyleena®[38] [Jaydess®]
This method "ticks more boxes" relating to the "ideal" contraceptive than any other option (JG). It also has added value: relieving PAIN[35] and/or menorrhagia, whether or not there is need for FP - facts about both symptoms that are still not widely enough appreciated! Like banded Cu IUDs, it is like sterilization for effectiveness. Therefore, when any form of sterilization is mooted, it is crucial to seek any history of heavy **OR** painful periods, maybe many years back, before the woman's long-term use of the Pill (or other hormonal contraception) improved them – see below, p 10 Col 2.

Other differences from copper IUDs are:
1 It acts potently but **slowly** compared to copper. So despite a promising study of IUSs used as EC (Turok *et al* https://tinyurl.com/2pwan9sx) the FSRH does not yet *recommend* IUSs for **EC**. Also, for non-EC insertions, it is ideal *routinely at counselling to advise an anovulant method to 'bridge' until the insertion time:* to reduce risk of exposure to uniquely high LNG levels if an unintended pregnancy occurred that might continue.
2 Mirena, but not as yet Levosert or Kyleena (below) is licensed for use as the progestogen component of fully *contraceptive* **HRT**: very popular, fully licensed and *the FSRH endorses its use thus for the full 5 years* (but UULP).
3 Women should be warned *to expect* that they will bleed on most days in the early weeks after insertion, but that if they are prepared to wait there will nearly always be the ideal outcome, of absent or light regular bleeding.
4 Some of the LNG gets into the blood, variably between women, and can cause progestogen-related side effects such as depression (shown in a million Danish women cohort to occur with *all* hormonal methods[39]). These usually improve as levels fall, in similar timescale - coincidentally - to the 'dribbling' of para 3 above. As a v rough approximation one can say Mirena/Levosert gives the blood levels of c 3 LNG POPs a week and Kyleena (below) equates to c 2 a week.
If **unacceptable bleeding** persists, or **returns much later**, first seek another cause (the **'D-Checklist'** [see Appendix]) - including *Chlamydia* and often a U/S scan for eg a uterine polyp, or malposition - then consider early replacement.

More about Levosert® Generically, this is LNG-IUS-52, where the 52 signifies its LNG content in mg. This is the same as Mirena® with which it is bio-equivalent though the insertion technique differs (while still straightforward, like the Nova T IUD). Its NHS price is lower and it is also (a big plus point in JG's view) becoming available at an even lower price to service-providers working in Africa. Since 2019 it has a 5-year contraception licence and the study to establish max. duration of use will continue for 7-plus years.



Kyleena®[38] Launched in UK in 2018, this is a mini-LNG-IUS with a smaller insertion diameter of 3.8mm (vs Mirena 4.4 & Levosert 4.8 mm). Insertion was significantly easier and with significantly less pain than insertion of Mirena. It has a 5-year licence with average release of 9 µg LNG /day versus 14 µg released by Mirena, hence is possibly though ***not*** yet proven to cause fewer progestogen-linked side effects. Periods are more likely to continue (although lighter than normal). A lower amenorrhoea rate may (or may ***not***) appeal to some women. This IUS can be a good alternative to Nexplanon for young women, including nulliparae, since acceptable bleeding patterns are more likely. But note:

Jaydess® *lacks any clear advantage compared with* Kyleena.

When might the same IUS be left in longer?
If fitted above age 45, and longer use is requested, the NICE **Guideline[27] as adapted by the Faculty of SRH permits for FP** (but NOT as part of HRT, see above), the sustained use of

the same IUS until contraception is no longer needed (UULP). ***If only for menorrhagia or pain control,*** not FP, the same IUS may of course be *in situ* for just as long as it continues to work, with one caveat (actinomycosis risk, see below).

What about LNG-IUSs and EIDs? Walli Bounds of Margaret Pyke Centre showed maintenance of *good* effectiveness in 50 users of the IUS plus enzyme-inducers (one pregnancy reported)[2]. This is biologically v plausible, since the LNG would still be released in high concentration ***locally,*** despite the EIDs lowering levels in the blood, and so should have its usual effects on the utero-cervical fluid and in impairing implantation. Therefore the LNG-IUS is a good alternative to DMPA (or a Cu-IUD) for women on EIDs.

PID risk? It is well established that ***neither IUDs (with monofilament threads) nor IUSs, intrinsically, increase PID risk***[1,2]**.** Yet neither can be relied on to *protect*. Moreover it is crucial to insert through a "Chinese cervix"! This is a cervix (or rather genital tract) established to be ***pathogen-free*** [see pp 113-117 of ref [1]], so far as it can ever be by screening: first a careful history for STI risk, PLUS if then indicated vulvo-vaginal swabs for *Chlamydia* - these give best sensitivity, even when self-taken[40]. **IF** a negative result is not available (eg when using a Cu IUD as EC), consider antibiotic cover, eg with azithromycin 1g stat; or, if lower-risk, ensure follow-up for possible later treatment. *Routine* IUC insertions with lowest estimated risk need no screening, nor antibiotic cover.

Ectopic pregnancy[2]? The absolute risk is *not* increased by use of any IUC. However it is clinically important that if they fail, the ratio of extra- to intra- uterine pregnancies is greater (through the paucity of the latter). With a **past history of ectopic, an anovulant method would be *even better*, but an IUS or ***banded*** IUD is **not** ruled out[2].

Some insertion-related tips for IUDs and IUSs[2] [JG]:

1 Always apply **"vocal local"**++; aka "verbal anaesthesia"! Diana Mansour [unpublished study, Newcastle] found that reported pain was least when a particular nurse assisted.

2 *When to insert?*

a. It is a *medical myth* that menstrual fitting (Days 1-5) is best. Expulsion rates are doubled[2] [White et al, 1980, see p 251 of ref 2 for more] and this is unsurprising, given ↑uterine activity during the *heavy* days of bleeding.

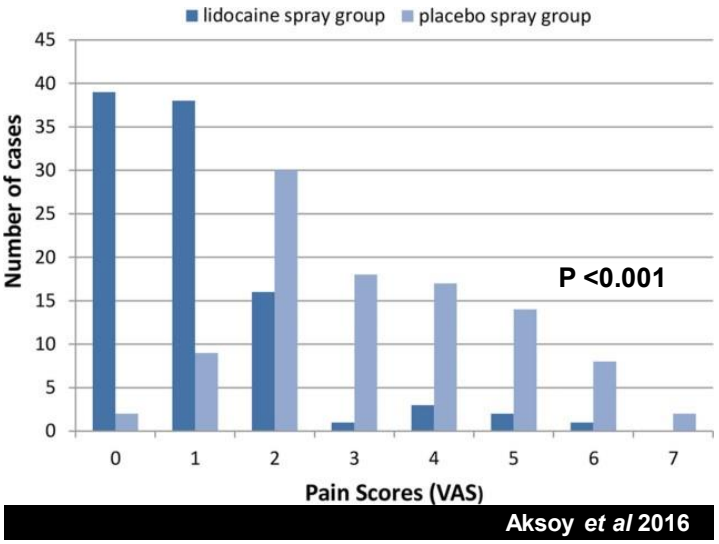
b. The risk of perforation (c 1-2/1000) increases to c 5-6/1000 during lactation.[2] This is not WHO 4, it signifies the need for *added care by an experienced provider* (WHO 2)

3 Insertion at the time of ***surgical**** *termination of pregnancy* is *ideal* wrt pain, given the already-present good LA or GA. Misgivings about expulsion rates, infections etc are over-stated[41]. Indeed IUCs can, and should, be ***offered*** **(**with easy opt-out) to all whose pregnancies end in the first trimester, since the ***parenteral*** **LARC ie (DMPA) seems less good** long term [requests for repeat terminations 2-5 years later are commoner than with IUCs (doi:10.1136/jfprhc-2014101059)]. Indeed, with full counselling before the day of surgery and solid agreement to remove the IUC later upon request, this must be the NORM!

* In ***medical*** *terminations,* IUCs are best fitted once products are confirmed expelled. More in FSRH guidance, URL on P 7 Col 2.

4 *Pre-medication* should be routine c 40-60 minutes beforehand. Mefenamic acid 500 mg helps to *pre-empt the uterine cramping pain* reported at 10 minutes after insertion[1]. Naproxen 500 mg (available OTC as Feminax Ultra®) has also been shown to help this pain, but oddly *not ibuprofen.*

5 **Some form of *anaesthesia to the cervix should be offered, to stop the*** very severe *sharp pain*[1,2] caused, *unpredictably,* in a few women by all types of holding forceps, which often then continues through the rest of the procedure. First choice is: (a) EMLA® cream or lidocaine 10% spray at least 3 minutes ahead. The spray as 3 puffs to the cervical surface and one into the external os was significantly effective in a 2016 RCT.[42]



See (2021): www.fsrh.org/standards-and-guidance/documents/fsrh-statement-pain-associated-with-insertion-of-intrauterine/

(b) Second choice now is *slow* inj. 2 minutes ahead of 1 ml of *warmed* LA, through a tiny needle, at 12 o'clock.

6 Re Instillagel® 2% LA gel using Instillaquill via Cx: the best studies strangely fail to show significant pain relief[43]. That was shown only with a stronger (lidocaine 4%) gel, not marketed[43]**.** IF the 2% gel is used, instil it *slowly* and ***wait*** *at least* 3-minutes. **But for routine practice JG advises as at 5** (a), above.

7 Paracervical LA injected at the level of the internal os is not necessary, routinely, but is effective[43] and should be used[2] if, rarely, the cervical canal needs dilatation to Hegar 5-6.

8 Beware: truly short cavities are rare. If the sound passes to ≤5cm it may only have measured the cervical canal.

9 Insertion is only considered 'complete' [JG - differing here from the FSRH] after a satisfactory first follow-up, at c 4-6 weeks. Thereafter, however, *there should be no routine visits.*

10 **NB: ANNUAL CHECK-UPS** are redundant for IUCs[1,2], according to WHO. Visits are at a user's choice – on an ***"open house"*** *basis, always immediate if she has* ***pain*** *[this being the No.1 'Red flag' symptom, with in IUC-users a serious cause* ***(such as PID, ectopic, malposition) till proved otherwise].***

Finally, ***expertise*** is of itself "analgesic". To maintain this, the FSRH advises a minimum of 12 insertions per year.

FEMALE STERILIZATION[44]? - OR BANDED copper IUD? - OR the IUS? - *efficacy is similar for all!* The Peterson et al study (1996)[1,2] showed the failure rate of *female sterilization in the USA at that time* to be 14/1000 at 7 years – not different from the rates for the T-Safe Cu 380A and the IUS by 7 years[34]. After that there were zero further failures with the banded copper IUD to 10 years (and the evidence shows this is extendable UULP to 12 years).

SO, why do a surgical procedure at all in many cases, when a banded IUD, or an IUS, is of equal efficacy, reversible and above 40 (or 45, see above) can be seen as permanent, never needing replacement during the finite and often quite short time between ending childbearing and Nature's ('auto'-) sterilization method, the menopause?

What about the Filshie clip? NB this was NOT used in Peterson's series above. The FSRH quotes its 10-year failure rate as 2-3/1000[44]; and of vasectomy as c 0.5/1000 after azoospermia.

VASECTOMY - deserves promotion! basing this usefully now on World Vasectomy Day (in 3rd week of November) and its website, plus the FSRH Guidance[44]. Using the much-to-be-preferred 'No-scalpel technique' and after nil sperm counts, its failure rate is 0.5-1:1000, decidedly more effective than the female procedures. But it shares a "risk": when either of the couple are sterilized, unacceptable menstrual symptoms often return due to discontinuing a previous CHC or other hormonal method. This is how *"vasectomy can cause menorrhagia!"*[2] - a term which only means "not tolerating one's menses". Certainly, whenever sterilization for either gender is mooted, one should never omit to ask the woman about her periods *as they were* prior to hormonal contraception, maybe many years before. If they were troublesome (sometimes in the history she was actually put on the Pill decades earlier to control menstrual symptoms!), an LNG-IUS might be altogether better than sterilization, whether male or female.

CONTRACEPTION & MEDICAL PROBLEMS[1,2]

Key guidance for many of these is at www.fsrh.org/ukmec/ They may be diseases or *"dis-eases"*: eg 'dysmen', or obesity https://tinyurl.com/v92xebtm But many rarer conditions have not been fully evaluated, so what principles apply?

A. Is there summation? *Are there disease-effects that are additive to known adverse effects of the method?*[2] If that is a CHC, for eg, does the condition increase thrombosis risk? Maybe by restricting mobility? even if otherwise unrelated to VTE.

B. Might the contraceptive worsen the condition? Eg Ca breast and hormonal methods. If there is no known summation ***and*** the disease itself is not suspected of being adversely affected by the contraceptive, the condition can be considered as at most WHO 2 for any method.
Otherwise, CHC use will be either WHO 4 or WHO 3.
NB: WHO 3 always implies *'an alternative preferable'*[1-2].

C. To decide between WHO 3 & 4 use clinical judgement: based on the concept of "resetting of the risk-balance": Even if a condition raises the risk of using a CHC, say, if there is *also an increased therapeutic benefit, the latter may make the carefully assessed risk-benefit difference similar to CHC-taking for contraception alone".* A common eg is PCOS + significant acne with BMI 35, acceptable despite WHO 3.
Importantly, in absolute terms added risk is the same as if the CHC was not being used thus, as treatment. It is wise to record that the patient understands and accepts this.

D. Also relevant, is an interacting drug used? See p 12 Col 1.

Acne/PCOS Acne, seborrhoea and sometimes hirsutism, with or without an established diagnosis of PCOS, may be benefited by any of the estrogen-dominant COCs (eg DSG+EE), but particularly by those with an anti-androgenic progestogen.
What now re Dianette© (co-cyprindiol)**?** In 2013-14, after the European (EMA) regulator's review triggered by VTE concerns in France, the MHRA advised UK clinicians that the estrogen-dominant products using CPA = Dianette© + its generic clones) and DSP (in Yasmin©) were **higher risk:** www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON287002
Yasmin® is a monophasic 21/7 COC containing DSP 3mg plus EE 30 µg. HOWEVER, a 20 µg ED variant **Eloine**® (DSG 3 mg +EE 20 µg), with the better regimen of 4-day CFI and 24 active pills, is now available[1,2]. Given its much lower dose of EE and evidence of similar acne-efficacy to Yasmin® this has become, since 2016, the first choice product [JG] for these conditions. Co-cyprindiol should always be second-line, reserved for non-responders and ceased after 'cure' - with switching for maintained benefit to, eg, a DSG + EE product. **Eloine**® is also a possibility for control of fluid-retention-linked side effects (DSP has a diuretic action). Moreover it is *licensed in the US for treating **PMS*, for which indication it clearly should be given continuously [JG]** - see above p 2 Col 2.
NB: feminisation of male fetuses has been shown (see SPC for Dianette®) in animal studies of CPA administered during embryogenesis. This must also be a *potential* risk with other weaker anti-androgens, DSP in Eloine or Yasmin, dienogest (in Qlaira[11]) & nomegestrol acetate in Zoely.
Therefore, with COC products using any of these:
<> at initiation, pregnancy must be confidently excluded
<> Bridge another pill first instead of quick-starting [see p 5]
<> *advise all: stop pill-taking if **any** suspicion of conception.*

Diabetes Mellitus (DM)
In general, and whether type 1 or type 2, this is always a WHO 3 *('alternative highly preferable')* condition for CHCs, given the higher circulatory disease risk even when there is no overt diabetic tissue damage [JG's view[1,2], yet UKMEC classes well-controlled diabetes as WHO 2]. DMPA is also WHO 3 [JG] in DM, given its SPC that reports a 15-20% reduction in HDL-cholesterol[2].
So the **POP (often a DSG POP), an implant, a modern copper IUD, or a LNG-IUS are all definitely preferred** to any of the CHCs. These can all be started any time after coitarche in young diabetics. If CHCs are, reluctantly, used, it should be for cases with no known arteriopathy, retinopathy, neuropathy nor renal damage, nor any added circulatory risk factor such as obesity or smoking (all of which then mean WHO 4) - and in my view only *if the duration of the disease has been less than 20 years*. Moreover the natural estradiol-containing Zoely[12] or Qlaira[11] are possibly safer (less prothrombotic) than products that use EE 20µg. Even these CHCs should be used with due caution (WHO 3), and with the plan to switch to a preferred method whenever acceptable; or perhaps sterilization after all childbearing.

Migraine with aura[1,2] Alone, this is a definite risk factor for ischaemic stroke, so WHO 4 for CHCs. However the data now suggest there is *no* clinically important added risk in *migraine without aura.*
What is aura?
Establish the **timing:** neurological symptoms of aura begin pre-any headache, typically last around 20–30 mins, max 60 mins, and resolve at about the start of the headache (which may be absent or mild). Premonitory symptoms like food cravings the day before are ***not*** aura.

Visual symptoms occur in 99% of true auras and hence should be asked about first.
Typically there is a bright loss of part of the visual field on the same side in both eyes (homonymous hemianopia)
Fortification spectra are described, a scintillating zigzag line usually observed even with eyes shut, gradually enlarging from a bright centre on one side, to form a convex C-shape around the area of lost vision (a bright not dark scotoma). **Sensory symptoms are highly confirmatory**, but occur in only about one third of cases and rarely in the absence of visual symptoms. Typically they come as 'pins and needles' (paraesthesia) spreading up one arm or one side of the face or the tongue; the leg is rarely affected. They are almost always positive symptoms, **not** loss of any motor or sensory neurological function (serious though that is - equally justifying stopping of the CHC, but also indicating urgent hospital referral). Disturbance of speech may also occur, in the form of dysphasia, again confirmatory of aura.
Aura *without headache* following is also WHO 4 for **CHCs**.
BUT all estrogen-free methods including all LARCs are OK for women with aura – warn them that the headaches may persist, the switching is for greater safety against stroke - and will be somewhat irrelevant if they continue to smoke!
How to take an aura history:
Ask the woman to describe a typical attack from the very beginning, including any symptoms in the 1-hour before a headache. Listen, but it is more important to watch her carefully. **A very suggestive SIGN of true aura is if she 'draws something in the air' to one or other side of her own head** (Anne MacGregor, as discussed in ref **2**).
In summary, aura has three main features: 1
TIMING: BEFORE or without headache, with duration ≤1 hour and disappearance before or at onset of headache
2 Symptoms VISUAL in 99 %, as described above
3 Description VISIBLE (patient waves, beside her head).

DRUG INTERACTIONS with contraceptive hormones
Here the FSRH Guideline[32] is particularly useful. Note that:
<> the cytochrome P450 enzymes of liver and gut wall are *induced* by enzyme-inducing drugs (EIDs), enhancing their activity and so reducing estrogen ***and*** progestogen blood levels. This is sustained for up to 28 days after EID cessation!
<> antibiotics pose *no problem*, generally, despite earlier concerns (*except* for rifampicin and rifabutin which are such potent EIDs that FSRH states an alternative *non-hormonal method* should routinely be advised).
<> in epilepsy,[26] the commoner EIDs are phenobarbital, phenytoin, primidone, carbamazepine, oxcarbazepine, eslicarbazepine, & topiramate *if daily dose above 200 μg*. NB For other conditions than epilepsy see Guideline[32] & BNF.
Management during use of enzyme inducers (EIDs):
<> During short courses *and for 28 days after cessation*, advise an added method such as condoms.
<> For medium to long-term treatments, unless the woman is prepared to continue use of that extra method, the recommended contraceptives include, as explained above, DMPA; also Cu IUDs and any of the LNG-IUSs.
NB: *not* Nexplanon. For the (hopefully few) women who insist on staying on a CHC or POP, there is a complex second-choice option involving high doses[32], and ideally continuous use if it is a CHC.[1,2] All these = UULP.
Interaction the other way, affecting Lamotrigine[1,32]
COC/CHC efficacy is not a clinical problem here, but blood levels of the lamotrigine itself can be lowered by EE, increasing the risk of a seizure after the Pill is commenced and, if this is compensated for, potential toxicity during the CFI. Co-administration is possible, with caveats[1]. But all CHCs are WHO 3 here: best to advise either an EE-free contraceptive or a different anti-epileptic regimen [JG]. Data currently suggest that progestogens do not have this effect.
Valproate - not an EID but it is a teratogenesis *nightmare!*
The URL www.gov.uk/government/news/**valproate**-banned-without-the-pregnancy-prevention-programme is prescriptive, that any woman in the childbearing years who needs valproate, or oral retinoid R_x must complete the annual Acknowledgment of Risk Form and use a ***best*** LARC. That category includes IUCs and implants, but NB excludes DMPA unless special terms are applied.

TEENAGE PREGNANCY [1,2]:
PREVENTION depends on use of the most appropriate contraceptives, but also on *much more:* please see the excellent Guidance from FSRH.[45] Table 1 below here gives **JG's ranking in 2022 of the first-choice methods** for a young person, whether teen or older. **NB *The user is the chooser: one moves down the list during counselling, to reach what must always be the user's own top choice.***

Table 1: Prioritisation of 'best' methods, for teens & older

1. **Depo** im **/SayanaPress**® sc acc to choice, then maybe move to SDI/Nexplanon when any xs bleeding settles, or at choice.
2. **SDI**® or **IUS.** [BTB problems less likely with latter]. Either fit SDI or IUS stat ie QS (p 4) ± LNG EC; or bridge first with a DSG-POP or *continuous* COC and fit 3 weeks(+) later at mutual convenience - IF pregnancy test –ve.
3. **Cu IUD**, probably put in as EC, often using the 'Slimline Mini' T-Safe Cu 380 A or ?IUB (p 5). ?IUS later if xs bleeding
4. **≤ 30 μg COC: by 365/[0] or tricycling regimen**, p 3 **OR,** and this might be initial plan, quick-started, ± LNG-EC (see p 6), bridging until start of a LARC when she is ready, at time convenient
5. **DSG POP** in consistent use is, through absence of CFIs, as effective as a COC taken 21/7! OTC availability now makes a highly effective method much more accessible to teens – p 4.
6. **NuvaRing CHC, best** using 10 rings/year & 365/[0], as p 4

Notes to Table 1 Prioritisation of methods for teens

<> If hormonal EC at 1st visit, QS still an option for SDIs.
<> But discuss which EC & if UPA explain protocol at p 6
<> Plus, outside of monogamy, advise/supply condoms for use prn *as well* and make available all 3 EC options.
<> At time of counselling for teens (or others) who request *surgical* termination of pregnancy, make the logical offer of IUD or IUS insertion at the procedure (p 10 col 1).

Counselling is made easier by www.contraceptionchoices.org, a site that tailors method choice to the user's own priorities (she can go to it independently, or with a provider during a consultation). For all methods QS as on p 4 is best, prioritising the LARCs.

But given her likely expectation is "the Pill", it is often ideal at first visit to ***bridge with*** **COC (obviously *NOT* given '21/7').** This also simplifies a **later planned switch to SDI? or IUC?**
Good news: there is some, re teen pregnancies. In 2017 the under 18 conception rate in England and Wales had fallen to 17.9/1000 [cf 47.1/100 in 1969!]. The downturn began after 2005, the launch date of a NICE Guideline on the LARCs, www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/conceptionandfertilityrates suggesting a probable causal association. However there are still more UK teen conceptions than in many other European countries, whose own rates have also fallen.

CONTRACEPTION FOR OLDER WOMEN [1,2]

"Menopause is usually a clinical diagnosis made retrospectively after 1 year of amenorrhoea. Most women do not require measurement of their serum hormone levels to make the diagnosis.[46]*"* However any advice to cease contraception needs to follow one of 3 plans, which are incorporated into Table 2 here. This is based on Table 8 of the excellent Guideline of the FSRH[45] which is essential reading and readily available at:
www.fsrh.org/standards-and-guidance/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/

Table 2 Recommendations re stopping contraception
[Table 8 of FSRH Guideline 2017[46], with some JG edits]

Contraceptive method	**Age 40–50 years**	**Age >50 years**
Non-hormonal (Barrier or IUD)	Stop FP after 2 years of amenorrhoea	**Plan A:** Stop FP after 1 year of amenorrhoea. No testing.
CHC	May continue, IF zero risk factors. A COC containing E2 is preferred.	Stop at age 50 with no testing & switch to a non-hormonal method or SDI/POP/LNG-IUS, then follow appropriate advice: ie Plan B or C⬇
DMPA im or sc	Can be continued to age 50 (WHO 2) But **stop** if FSH is ≥ 30 IU/L, pre-next dose	Stop by age 50 with no test & switch to a non-hormonal method or SDI/POP/LNG-IUS, then follow appropriate advice: Plan B or C⬇ below
(SDI (POP (LNG-IUS	Can be continued to age 50 and beyond	**Plan B** With no FSH test stop at age 55 when natural loss of fertility can be assumed for most women**.
IF a woman is amenorrhoeic and wishes to stop any of these FP methods over 50 but *before* age 55, consider this **Plan C**	n/a	**Plan C** FSH level can be checked while on method: If FSH level is >30 IU/L, after 1 final year the woman may then simply discontinue her hormonal FP; but must report IF against expectation, she has any later bleed. *However:* If FSH level is ≤ 30 IU/L the method should be continued and FSH level checked again in 1 year.

** Re Plan B, see JG text below re **option** of an assessment time of c 8 weeks using a simple FP method, before giving the "all clear".

<> **Plan A.** After age 50, after stopping any sex hormones: do not discontinue FP until after for the 'officially approved' one year of amenorrhoea. This is the obvious plan for deciding when to discontinue copper IUDs or condoms, since they do not hide the menses. **But what to do if the woman is on one of the hormonal methods, or HRT** (a separate issue and it is of course not contraceptive), **which mask the menopause?**
If on DMPA im or sc, or any CHC (that only being acceptable if risk-factor-free), age above 50 - the *mean* age of the menopause is c 51 years - is the usual latest time to switch to something else. The known risks though rare of CHCs go up with age, *even in totally risk-factor-free women and even if, as now seems logical and preferred for most such, they recently have been taking natural estrogen* (Zoely or Qlaira). CHCs are also by age 50+ needlessly 'strong', contraceptively. The same applies to **DMPA.** Here the switch to eg an SDI, POP or LNG-IUS can be made as in Table 2 without an FSH test - the Guideline rightly says FSHs are very rarely indicated before 50. However a FSH result of >30 IU/L if done (logically) just prior to the next DMPA injection is clinically meaningful, so may then be followed by one of the three acceptable menses-masking methods above, for a full year. This duration is important as, ***if*** an ex-DMPA-user has any residual fertility, ovulation might resume after a prolonged delay – like at younger ages.
POPs, or implant (SDI), or LNG-IUSs:
These, though similarly menses-hiding contraceptives, cause negligible medical risks well into the 50s. So for them it is entirely acceptable to follow the next plan, Plan B.

<> **Plan B. Switch to or continue with one of the latter, *progestogen-only contraceptives* and then just stop when the latest age of potential fertility is reached.**
When is that latest fertile age? A good guess is age 55, because, as the FSRH Guideline[46] states:
"…spontaneous conception after this age is exceptionally uncommon even in women still experiencing some menstrual bleeding" - and a large majority will anyway continue amenorrhoeic after stopping hormonal FP. However a small minority of c 4 % (a figure based on work in the 1960s, so maybe a few % more with greater average health these days) may have seemingly normal cycles beyond 55. Hence after ceasing or removing** the masking hormonal method, JG advises use for 8 weeks of a simple method. Gygel spermicide via applicator should suffice, due to minimal residual fertility at this age [JG], and generally can cease after the 8 weeks. Those *very* few who bleed during those 8 weeks (or report, as they should, any bleeds later on) are advised:
<> to continue with spermicide or barrier contraception and report back when their periods *finally* seem to have ceased. **OR:**
<> to go back on POP/SDI which have no age-related risks.
Any bleeding after ceasing FP that meets the criteria for PMB (see Glossary) needs appropriate investigation[2].
NB: FSH testing is usually unhelpful, for diagnosis of loss of ovarian function**!** Hence, *neither* of the above plans propose using FSH for any guidance re final ovarian failure.

****

**** Footnote re removing IUSs:** NB, despite possible pressure to leave it alone, it is advisable to remove an LNG-IUS, indeed any IUCs after this age. If IUSs or Cu-IUDs are left *in situ* post-menopausally there are case reports of severe infections later, including florid actinomycosis.

<> **Plan C**: see p 13 Table 2, Col 3. This is for continuing users of a hormonal method who have reached age 50-plus and want to learn sooner than by Plan B if they may - or contrariwise *should not* - discontinue contraception.
Opposite (Col 2) there is a JG variant of Plan C which may interest a few women, namely those who do not wish to continue their SDI/POP/IUS for the one further year advised in Table 2.
Note: Above age c 51, any 'medical' method may be quick-started, see Box p 4, in almost all cases. This is because annual risk of conceiving then is so low above 50, < 2/100 women - higher only if there are still regular cycles.

****

<> **Alternative Plan C**[2] Provided they have classical vaso-motor symptoms and **two** high FSH values 6 weeks apart, along with (as usual) due warnings of lack of 100% certainty, women may cease FP right then, age 50-1. However they should understand that to follow the rule of one-final-year of FP would be 'even safer', contraceptively. And *should any later bleeds occur, rarely*, they must undertake to return to good FP and take urgent advice re the possibility of PMB.
[There is more on p 352 of Ref 2].

****

Finally, see below for:
25 messages which may change your practice
(or maybe not, if you were already up to speed!)
[NB: in page order, **not** in any order of importance]

- Recommend to all prospective users the website www.contraceptionchoices.org and also consider using it routinely during most contraceptive consultations
- COC-taking with pill-free intervals *absent* or *short*, ≤ 4 days, to become the NORM - pp 1-3
- If COC is WHO 3 on the WHO/UKMEC Medical Eligibility Criteria: consider Zoely® or Qlaira® since they contain E2 natural estradiol - p 3-4
- NuvaRing® = option to R_x BTB with COCs - p 4
- Quick-starting or Bridging to be the NORM now *esp.* after hormonal EC [LNG-EC] - p 5
- **BUT,** preferably do not quick-start with anti-androgenic progestogens or if fitting an IUS - p 5
- **BUT,** post UPA for EC, wait 5 days and only then start any progestogen, alone or combined with EE - pp 6
- The 'Proving not Pregnant Protocol' with Bridging: helps when there is no LMP; but also avoids that *logistic nightmare* of ensuring LARC starts are pre-D7 - Box, p 5
- Cu IUDs are the most effective EC (failure rate 1:1000), till D 5 post-ovulation, based on the shortest likely cycle, despite multiple UPSI. FP continues until, and may also of course suit well beyond, the NMP - pp 5-6
- Be seated and observe needle bevel during Nexplanon® insertion and use enough-but-minimum LA - p 7-8
- NET 1 mg (1000 µg) metabolises to give 4 µg of EE, therefore Primolut N® 5 mg tds for bleeding symptoms or to postpone periods equates to a high-dose COC - p 8
- Sayana Press® is DMPA sc and close to same cost as Depo-Provera, and moreover is self-injectable, aided by a web-based animated film - p 8
- *Banded* copper IUDs and IUSs are arguably the *best of the best* among FP methods - pp 8-10
- 1st choice of Cu IUD *now* = **Mini** TT 380 Slimline - p 9
- IUSs as alternative to Nexplanon®, if bleeding pattern is unacceptable - pp 7, 9
- FP post-*surgical* abortions: ideally to propose an IUD or IUS and this to be a new NORM when counselling - p 10
- Pain relief for IUC insertions by naproxen or mefenamic acid + the value of 10% lidocaine spray to the surface and into cervical canal - p 10
- No *routine* follow-ups: "Open house" policy is preferred for IUDs and IUCs, indeed most methods - pp 8, 10
- Vasectomy should, routinely, be done only by a "No scalpel" technique - p 11
- Eloine® usual 1st FP choice now for acne, ***not*** Yasmin®. Dianette® (or clone) = 2nd choice when necessary - p 11
- Migraine aura, how to diagnose: by *hand-waved-by-head* whenever patient describes it - p 12
- Lamotrigine: ethinylestradiol in COCs may cause this to fail (hence seizure risk) - p 12
- Remember: www.gov.uk/government/news/**valproate**-banned-without-the-pregnancy-prevention-programme - p 12
- To establish ovarian failure at menopause if current use of a menses-masking method: see Table 2 - p 13
- 'D' Check-list for unwanted bleeding, with COCs - but other methods too – see Appendix p 15

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[Comments re this document are invited, via email as above]

APPENDIX

WHO Medical Eligibility Criteria or **UKMEC,** the UK adaptation www.fsrh.org/standards-and-guidance/documents/ukmec-2016/

CATEGORY [with JG's ABCD added]	**BECAUSE:**
WHO 1 - or A for *Always* usable	**No associated risks**
WHO 2 - or B for *Broadly* usable	**Benefits > risks**
WHO 3 - or C for *Caution/Counsel**	**Risks usually > benefits**
	* Starting point for that 'Counsel' is: "it would be better not to use this method" ie say it's not recommended *unless* other more appropriate methods are not available or not acceptable, and taking account of woman's risks in pregnancy
WHO 4 - or D for *Do not use*	**Risks >>> benefits,** an unacceptable health risk

The D-checklist for abnormal bleeding in a COC-user: from Contraception Today 9th Ed (2020) p 70

- **DISEASE**: Consider examining the cervix. Is the BTB due to *Chlamydia* or a polyp (or cancer?), or rarely a congenital bleeding disorder?
- **DISORDERS of PREGNANCY** that cause bleeding. Threatened early miscarriage? Could it be early in gestation of an ectopic pregnancy? Or, retained products if COC was started stat after a recent termination of pregnancy?
- **DEFAULT**: BTB 2 or 3 days *after* missed Pills episode and persistent thereafter.
- **Diarrhoea and/or VOMITING:** Diarrhoea alone has to be "cholera-like" to impair absorption.
- **DRUGS,** if they are enzyme inducers (see text). Cigarettes are also "drugs": BTB is more common among smokers.
- **DISTURBANCES of ABSORPTION:** For example, after massive gut resection (rare).
- **DURATION of USE** too short: BTB after starting on any new formulation may settle, if the 21/7 pill taker perseveres for 3 months. However during tricycling or 365/[0] sustained use, the duration of continuous use may be such that that woman's endometrium is unstable, in which case a 4-day bleeding-triggered break may be usefully taken (see text).
- **DOSE**: After the foregoing have been excluded, it is possible to try
  - A phasic Pill if the woman is receiving monophasic treatment.
  - Increasing the dose, usually of the progestogen OR: A different progestogen OR:
  - **NuvaRing**® might be tried, which in RCT produced less BTB/spotting in the first year than Microgynon 30[1,2].

Importantly, this check-list is also applicable to other hormonal methods (eg POPs, SDIs, injectables), with the obvious adaptation that 3rd & 4th bullets do not apply to any non-oral route.

Acknowledgement: expanded from Sapire E. *Contraception and Sexuality in Health and Disease.* New York: McGraw-Hill, 1990.

GLOSSARY

AF atrial fibrillation / **BMI** body mass index / **BTB** breakthrough bleeding+spotting **CFI** contraceptive-free interval / **CHC** combined *hormonal* contraceptive(s) / **C-Is** contraindications / **COC** combined *oral* contraceptive(s) / **CPA** cyproterone acetate / **Cx** cervix / **DM** diabetes mellitus / **DMPA** depot medroxyprogesterone acetate, either as Sayana Press or Depo-Provera / **DSG** desogestrel / **DSP** drospirenone/ **E2** estradiol / **EC** emergency contraception / **EE** ethinylestradiol / **EID** (liver) enzyme-inducing drug / **EMA** European Medicines Agency / **FP** family planning (method) / **fpa** Family Planning Association / **FSH** follicle-stimulating hormone / **FSRH** Faculty of Sexual and Reproductive Health / **GSD** gestodene / **IU** international unit(s) / **IUC (IUB)(IUD)(IUS)** / intrauterine contraceptive (ball)(device)(system) / **im** intramuscular / **SDI** subdermal implant (Nexplanon) / **LA(GA)** local (general) anaesthesia / **LAM** lactational amenorrhoea *method* / **LARCs** long-acting reversible contraceptives / **LMP - NMP** last - *next* menstrual period / **LNG** levonorgestrel / **NET** norethisterone / **NICE** National Institute for Health & Care Excellence / **NSAID** non-steroidal anti-inflammatory drug / **OTC** over the counter, product sold direct to consumer / **PFI** pill-free interval / **PGD** patient group direction/ **PIL** patient information leaflet/ **PK** pharmacokinetic / **PMB** post-menopausal bleeding, occurring after 6/12 amenorrhoea / **PMS** premenstrual syndrome / **POP** progestogen-only pill / **QS** quick-start(ing) / **RCOG** Royal College of Obstetricians & Gynaecologists / **RCT** randomised controlled trial / **sc** subcutaneous / **SDI** subdermal implant / **SEs** side effects / **SPC** Summary of Product Characteristics / **SRH** Sexual & Reproductive Health / **STI** sexually transmitted infection(s) / **UKMEC** UK Medical Eligibility Criteria / **UPA** ulipristal acetate / **UPSI** unprotected sexual intercourse / **UULP** unlicensed use of a licensed product [NB where used unqualified, here, **UULP** means ***"follow the GMC approved criteria in the box on p 1"***] / **U/S** ultrasound / **VTE** venous thrombo-embolism / **WHO** World Health Organisation.

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SOME 'BELIEVABLE' WEBSITES IN SRH

- www.contraceptionchoices.org
  Best website [JG] for ANY woman deciding between her FP options
- www.margaretpyke.org
  London local services, FP research, and Training Courses on offer
- www.who.int/reproductive-health
  Access to WHO's invaluable e-publications including latest Eligibility criteria & Practice recommendations, also the Global Handbook on FP
- www.rcog.org.uk
  Evidence-based College Guidelines on infertility and menorrhagia
- www.fsrh.org
- Website of FSRH, includes numerous Faculty Guidance pdfs re FP, male & female sterilization, access to the Journal, UK MEC Tables and more
- www.nice.org.uk
  Particularly useful for its LARC & Menopause Guidelines
- www.brook.org.uk
  Similar to fpa website but for < 25s; plus a secure on-line enquiry service. Helpline 0800 0185023
- www.fertilityuk.org
  The best URL re fertility awareness methods, for clinicians & for couples.
- www.bashh.org
  National guidelines for all STIs & listing of GUM Clinics in the UK
- www.gmc-uk.org/guidance/ethical_guidance/children_guidance_index.asp
  Ethical guidance for all doctors, on all that relates to the age-group 0-18
- https://www.sexwise.fpa.org.uk/
  www.scarleteen.com [US site]
  These are user-friendly, accurate, and empowering for young people accessing SRH – whether for FP or STIs
- www.familylives.org.uk/ [formerly parentline plus]
  Top tips for parents, to help teens/pre-teens avoid many kinds of grief
- www.ecotimecapsule.com[1] & www.populationmatters.org[2]
  [[1]This describes JG's 'Apology to the Future' project and contains his ***"The Promise"*** video + useful pdfs (Handouts) and slides.
  [2]This contains JG's pdf on teen pregnancy entitled Y*outhquake*]

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  <> www.condomoutlet.co.uk:
  for all options including modern oil-resistant plastic condoms.

JG, September 2022