

## FSRH CEU Statement: Response to Recent Publication Turok et al. (2021) “Levonorgestrel vs. Copper Intrauterine Devices for Emergency Contraception”

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A study published in the New England Journal of Medicine<sup>1</sup>, suggests that a 52mg levonorgestrel-releasing intrauterine system (LNG-IUS) is non-inferior to a T380A copper IUD (Cu-IUD) for emergency contraception (EC).

**Background.** The Cu-IUD is much more effective for EC than oral EC.<sup>2</sup> The LNG-IUS is not currently used for EC because published evidence of its effectiveness for this indication is lacking. Some individuals that decline a Cu-IUD for EC because they would not wish to use the Cu-IUD for ongoing contraception might accept an LNG-IUS in this situation because of its non-contraceptive benefits.

In some parts of the world, including the USA (but not the UK) individuals receiving levonorgestrel oral EC (LNG-EC) after UPSI can quick start the LNG-IUS at the same time. A previous study<sup>3</sup> (also by Turok et al) indicated user preference for the LNG-IUS over the Cu-IUD in this situation and reported no pregnancies amongst 121 individuals requiring EC who took LNG-EC and also quick started a 52mg LNG-IUS.

The authors of the current study postulate that the LNG-IUS would be effective for emergency contraception because of the known ability of levonorgestrel to “directly interfere with sperm transport, sperm capacitation, the acrosome reaction, and oviduct transport”.

**What happened in the new study?** Conducted in the USA, the study randomised 711 individuals who requested EC to receive either a T380A Cu-IUD or a Liletta<sup>®</sup> 52mg LNG-IUS (equivalent to Levosert<sup>®</sup>) for EC at no cost to the participant. Study participants:-

- ▶ had a negative urine pregnancy test
- ▶ had had at least one episode of UPSI in the previous 5 days
- ▶ had not taken oral emergency contraception in the previous 5 days
- ▶ could also have had UPSI at any other time since the start of their last menstrual period (LMP)

To be eligible for inclusion in the study, subjects had to be aged 18-35 years, have regular menstrual cycles and know the date of their LMP (+/-3 days). Individuals were excluded from the study if they were breastfeeding, currently using highly effective contraception (an intrauterine method, subdermal implant or sterilisation), or had had a recent pelvic infection or chlamydia or gonorrhoea. Of the 10,317 individuals seeking EC who were assessed for eligibility, 80% declined to take part in the study and a further 13% did not meet study criteria.

The groups randomised to use of each of the two interventions were very similar, but they differed in the reason given for seeking EC. In the LNG-IUS group, fewer subjects had used no contraception at the time of last intercourse (40.7% vs 50.5% in the Cu-IUD group), more subjects reported a condom accident (18.8% vs 12.5%) and more had run out of contraception or missed a dose (4.6% vs 2.4%).

### What were the study findings?

**LNG-IUS group.** There were 21 failed LNG-IUS insertions. Of the 327 subjects that received the LNG-IUS, 6 were lost to follow up and 4 discontinued the study. Amongst the remaining 317 subjects, urine pregnancy test results a month later were available for 290; pregnancy outcomes for 27 were obtained by later survey or examination of health records. **One pregnancy was recorded, in an individual who had reported one episode of UPSI 48 hours prior to insertion of the LNG-IUS.**

**Cu-IUD group.** There were 20 failed Cu-IUD insertions. Of the 328 subjects that received the Cu-IUD, 6 were lost to follow up and one withdrew from the study. Amongst the remaining 321 subjects, urine pregnancy test results a month later were available for 300; pregnancy outcomes for 21 were obtained by later survey or examination of health records. **No pregnancies were recorded.**

Ten individuals in the Cu-IUD group and 12 in the LNG-IUS group discontinued use within a month of insertion. Method satisfaction was high and the number of reported adverse events was low in both groups.

**What can be concluded from this study?** The study reports a pregnancy rate of 0.3% (95% confidence interval (CI) 0.01 to 1.7) in the LNG-IUS group and 0% (95% CI 0 to 1.1) in the Cu-IUD group. The between-group difference was 0.3% (95% CI -0.9 to 1.8). The authors conclude that the study demonstrates non-inferiority of the 52mg LNG-IUS for EC compared to the Cu-IUD.

There are, however, some limitations to the presented evidence that should be taken into account when considering how the study findings guide clinical practice.

- ▶ Of the 10,317 individuals seeking EC that were assessed for eligibility, only 7% were entered into the study (80% declined to take part in the study and 13% did not meet study criteria); this could have resulted in selection bias such that study participants may not be representative of the population requesting EC.
- ▶ The indication for use of EC in the LNG-IUS group differed from that in the Cu-IUD group – this could reflect different baseline risk of pregnancy.
- ▶ The presented data do not allow any assessment to be made as to whether UPSI had taken place at a time when risk of pregnancy was likely to be high.
- ▶ Pregnancy outcomes are unknown amongst those that withdrew from the trial or were lost to follow up after the intervention – this was the case for about 3% of subjects that received an LNG-IUS and 2% of those that received a Cu-IUD. In a further 8% of the LNG-IUS group and 6% of the Cu-IUD group, pregnancy test results a month after the intervention were not available; outcomes were inferred by checking clinic records and later survey responses for reports of pregnancy.

### How does this affect practice?

**The FSRH CEU recommends no change to current practice at this time.** The presented findings do, however, suggest that the 52mg LNG-IUS could be an effective method of emergency contraception, and further research is encouraged. The study adds to a growing body of evidence that could potentially support quick start of the LNG-IUS at the time of administration of LNG-EC or in situations in which a pregnancy test is negative but there has been UPSI in the last 21 days.

**The Guideline Development Group for the next update of FSRH Guidelines Intrauterine Contraception and Emergency Contraception will consider whether there is adequate evidence to support changes to current recommendations.**

### References

1. Turok DK, Gero A, Simmons RG, Kaiser JE, Stoddard GJ, Sexsmith CD, Gawron LM, Sanders JN. Levonorgestrel vs. Copper Intrauterine Devices for Emergency Contraception. *New England Journal of Medicine* 2021;**384**(4):335-44.
2. Faculty of Sexual & Reproductive Healthcare. *Emergency Contraception*. March 2017, amended December 2020. Available online [here](#) (accessed 08/02/2021)
3. Turok DK, Sanders JN, Thompson IS, Royer PA, Eggebroten J, Gawron LM. Preference for and efficacy of oral levonorgestrel for emergency contraception with concomitant placement of a levonorgestrel IUD: a prospective cohort study. *Contraception* 2016;**93**(6):526-32.

*The Clinical Effectiveness Unit (CEU) was formed to support the Clinical Effectiveness Committee of the Faculty of Sexual & Reproductive Healthcare (FSRH), the largest UK professional membership organisation working at the heart of sexual and reproductive healthcare. The FSRH CEU promotes evidence based clinical practice and it is fully funded by the FSRH through membership fees. It is based in Edinburgh and it provides a members' enquiry service, evidence-based guidance, new SRH product reviews and clinical audit/research. [Find out more here.](#)*