New in Contraception

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Unintended pregnancies

- World-wide about **99 million** unintended pregnancies occur each year :
  44% of all pregnancies.
- > 1/2 of these unintended pregnancies end in an induced abortion :

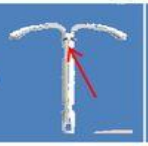
  56 million per year

LNG-IUS

- **Mirena** 52 mg -5 years
- **Levosert** 52 mg -5 years
- **Kyleena** 19.5 mg -5 years
- **Jaydess** 13.5 mg -3 years

Mirena, Kylena, Jaydess

Mirena, Kyleena and Jaydess

	Mirena 	Kyleena 	Jaydess 
Total LNG content	52,0 mg	19,5 mg	13,5 mg
Initial in vivo LNG release rate	20 µg/day	17,5 µg/day	15 µg/day
T-frame dimensions	32 x 32 mm	28 x 30 mm	28 x 30 mm
Insertion tube diameter	4,75 mm	3,80 mm	3,80 mm
Maximum duration of use	5 years	5 years	3 years
Silver ring included	no	yes	yes
Colour removal threads	brown	bleu	brown

Kyleena, Mirena, Levosert, Jaydess

Table 1: Product characteristics of Kyleena, Mirena, Levosert and Jaydess.

Type of LNG-IUS	Kyleena[3]	Mirena[4]	Levosert[5]	Jaydess[6]
Total LNG content (mg)	19.5	52	52	13.5
LNG release rate (mcg/24h) Initial Final Average	 17.5 7.4 (after 5 year) 9 (over 5 years)	 20 10 (after 5 years) 14 (over 5 years)	 19.5 9.8 (after 5 years) 14.7 (over 5 years)	 14 5 (after 3 years) 6 (over 3 years)
Frame size (W x H, mm)	28 x 30	32 x 32	32 x 32	28 x 30
Inserter	One handed EvoInserter™	One handed EvoInserter™	Two-handed inserter	One handed EvoInserter™
Insertion tube diameter (mm)	3.8	4.4	4.8	3.8
Silver ring for improved visibility on USS?	Yes	No	No	Yes
Colour of threads	Blue	Brown	Blue	Brown
Licensed duration of use for contraception (years)	5	5	5	3

Continue next page

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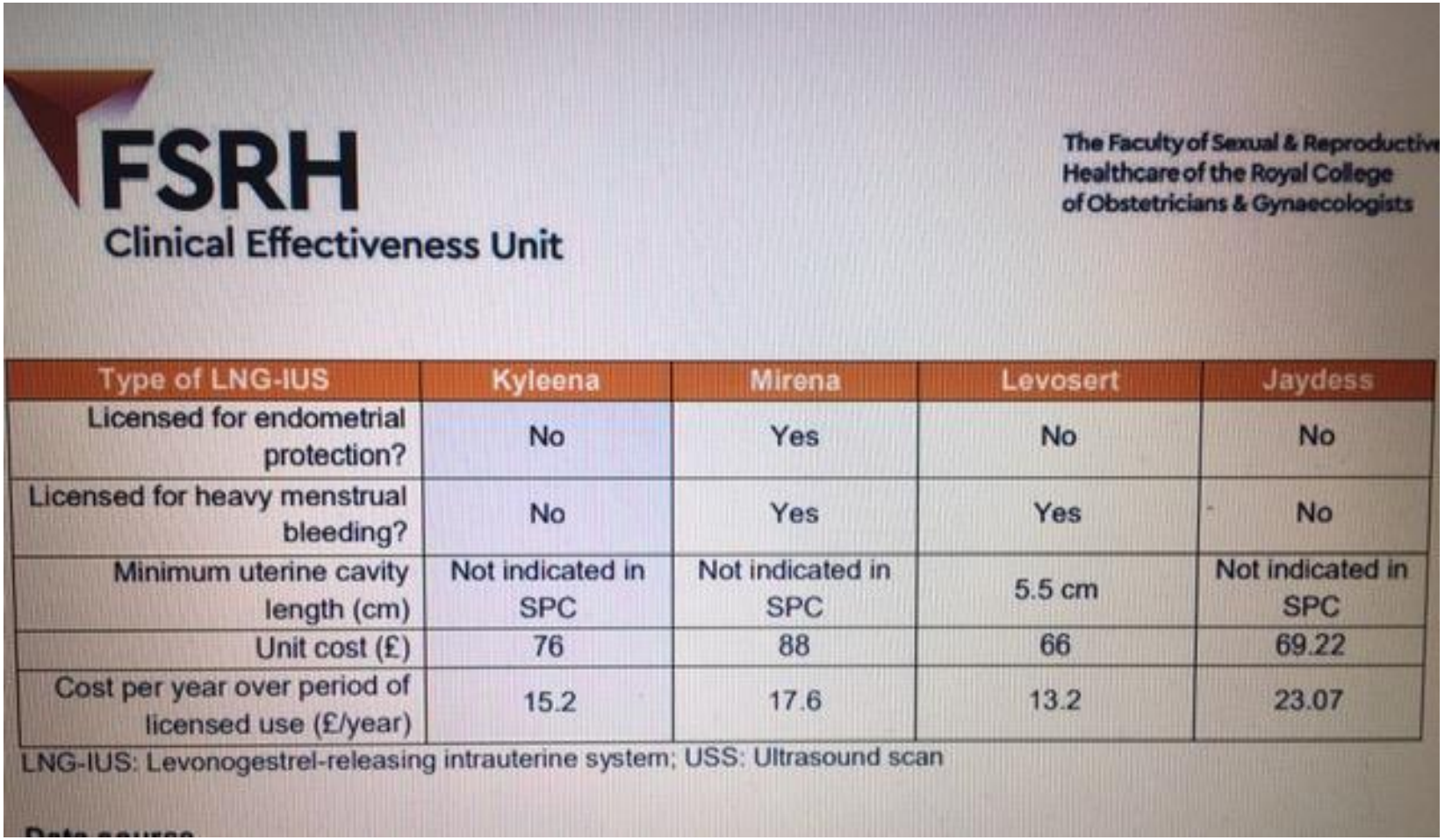
Kyleena, Mirena, Levosert, Jaydess



FSRH
Clinical Effectiveness Unit

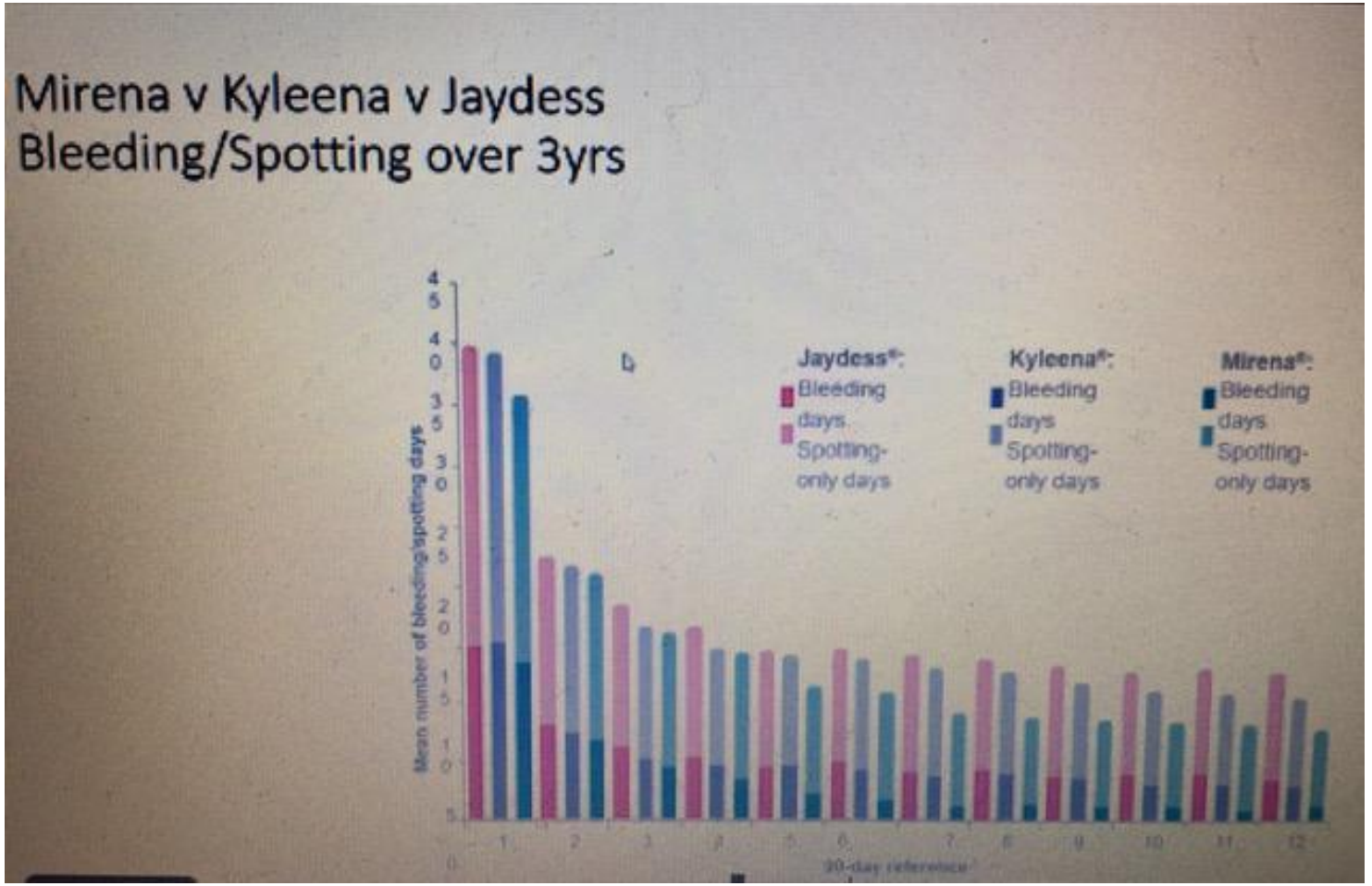
The Faculty of Sexual & Reproductive Healthcare of the Royal College of Obstetricians & Gynaecologists

Type of LNG-IUS	Kyleena	Mirena	Levosert	Jaydess
Licensed for endometrial protection?	No	Yes	No	No
Licensed for heavy menstrual bleeding?	No	Yes	Yes	No
Minimum uterine cavity length (cm)	Not indicated in SPC	Not indicated in SPC	5.5 cm	Not indicated in SPC
Unit cost (£)	76	88	66	69.22
Cost per year over period of licensed use (£/year)	15.2	17.6	13.2	23.07

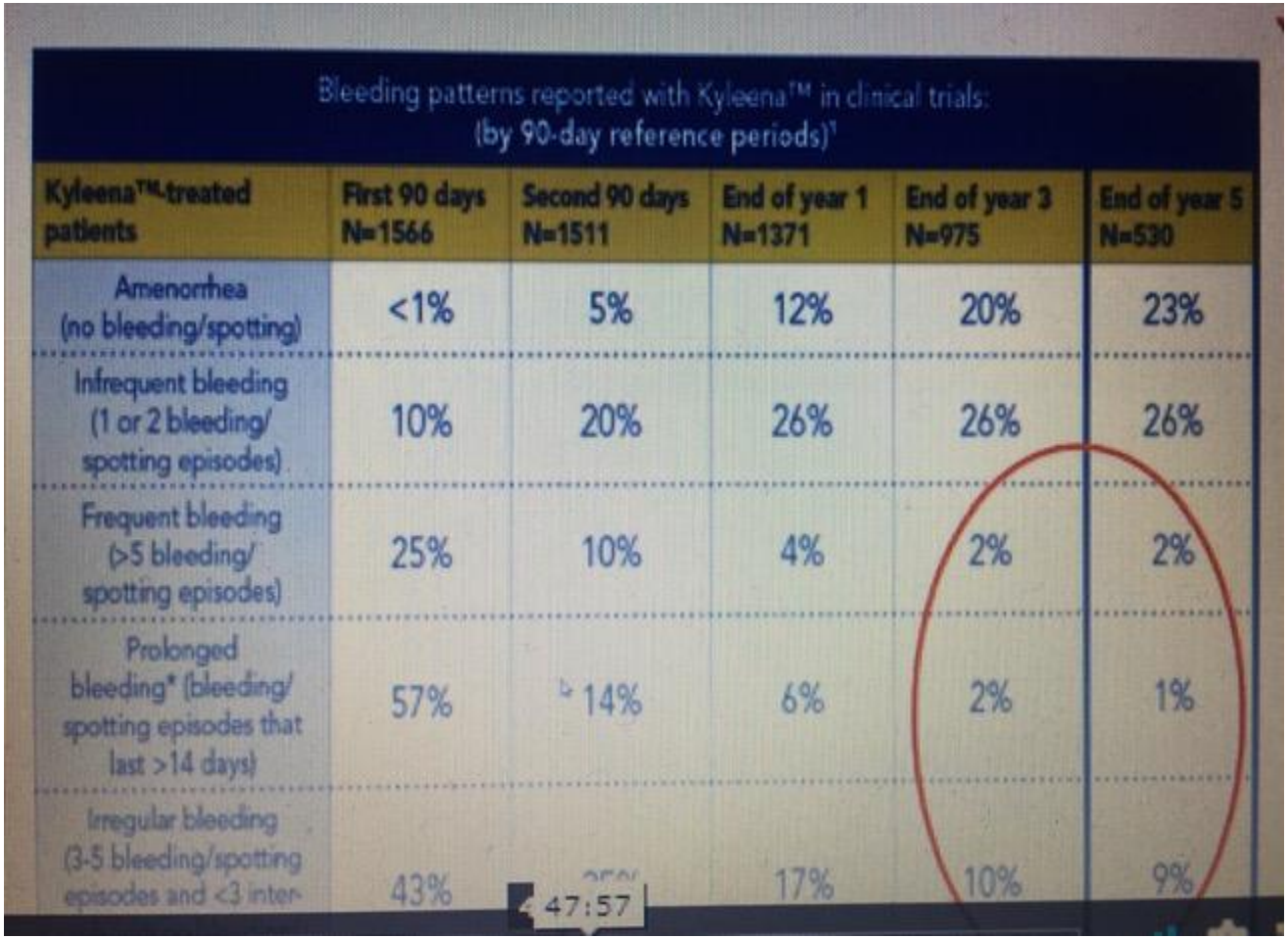
LNG-IUS: Levonogestrel-releasing intrauterine system; USS: Ultrasound scan

Data source

Bleeding/spotting over 3 years



Kyleena bleeding



Bleeding patterns reported with Kyleena™ in clinical trials:
(by 90-day reference periods)[1]

Kyleena™-treated patients	First 90 days N=1566	Second 90 days N=1511	End of year 1 N=1371	End of year 3 N=975	End of year 5 N=530
Amenorrhea (no bleeding/spotting)	<1%	5%	12%	20%	23%
Infrequent bleeding (1 or 2 bleeding/ spotting episodes)	10%	20%	26%	26%	26%
Frequent bleeding (>5 bleeding/ spotting episodes)	25%	10%	4%	2%	2%
Prolonged bleeding* (bleeding/ spotting episodes that last >14 days)	57%	14%	6%	2%	1%
Irregular bleeding (3-5 bleeding/spotting episodes and <3 inter-	43%	[illegible]	17%	10%	9%

47:57

Levosert® 52mg LNG-IUS licensed

- for contraceptive use for **6 years**
- for **5 years** for management of heavy menstrual bleeding

Levosert. How does this affect practice?

- Users of the Levosert 52mg LNG-IUS can now be advised that the device can be used as highly effective contraception for **6 years**.
- Levosert remains **unlicensed for use for endometrial protection as part of HRT**.

Extended use of 52 mg IUS to 6 years

- Involves discussion with pt
- Fitted > 45 y o can stay until 55 y o

LNG-IUS & menorrhagia

- **Mirena** for endometrial protection for 5 years for HRT
- **Levorsert**-out of licence for endometrial protection, and can be use until age 55

It is still licensed for menorrhagia for 5 years (although FSRH guidance is that it can be retained for longer if the menorrhagia is controlled), but it is not licensed for HRT

Mirena & Levorsert: in house rules

- We should continue with Mirena IUS in the 45 & overs, but
- To use Levosert as first line in women under 45.
- This is in line with other regional services.

IUD

- 10 y IUD extended to 12 year

COVID restrictions

- Extended use of Mirena and Levosert Risk of pregnancy during the **6th year** of use of a 52mg LNG-IUS appears to be very low, but evidence is limited.
- See FSRH CEU recommendation on extended use of the etonogestrel implant and 52mg levonorgestrel-releasing intrauterine system **during COVID restrictions**

Pandemic's rules: IUS replacement

During the COVID-19 pandemic, when replacing*:

Mirena, Levosert, Kyleena in situ for up to 5 y,

Jaydess in situ for up to 3 ys or

a Cu-IUD within its licence – **PT is NOT required**, no additional contraceptive precautions are required after replacement.

Pandemic's rules: IUS replacement

Mirena or Levosert in situ for up to **7** years or **10-year Cu-IUD** that has been in situ for up to **12** years – so long as **PT is negative**, replacement can proceed, with advice to use **condoms for 7 days** and to take a follow up urinary **PT at 21 days** after the last UPSI.

Pandemic's rules: IUS replacement

Mirena or Levosert in situ for **>7** years,

Kyleena in situ for **> 5** years,

Jaydess in situ for **>3** y,

5 year Cu-IUD in situ for **> 5** years or

10 year Cu-IUD in situ for **>12** years –

a **negative PT after 3 weeks of additional contraceptive precautions is required** prior to replacement;

condoms should be advised for 7 days after replacement of Mirena/Levosert/Kyleena/Jaydess.

FSRH CEU Statement

Response to Recent Publication Turok et al. (2021) “Levonorgestrel vs. Copper Intrauterine Devices for Emergency Contraception” 9 February 2021

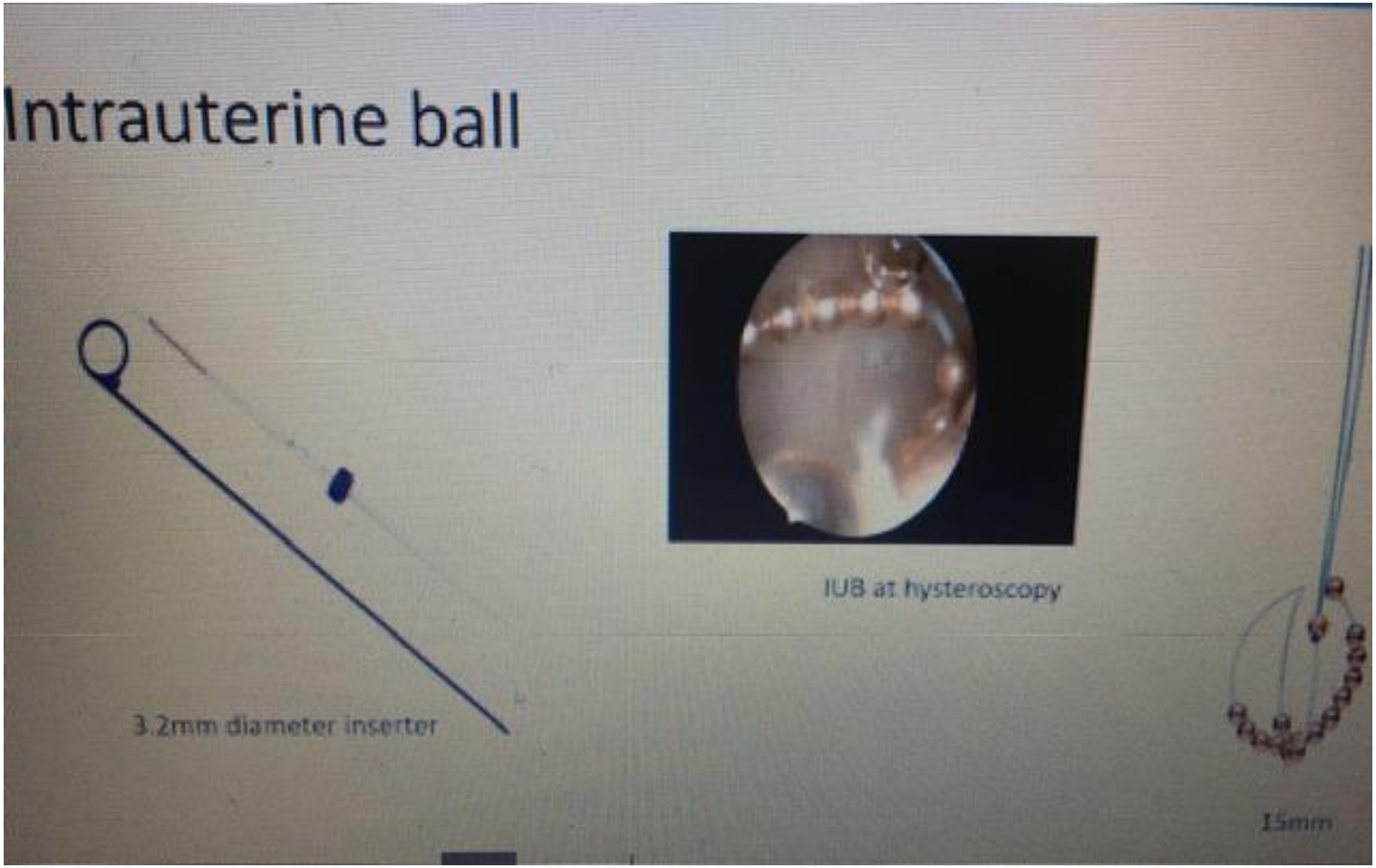
How does this affect practice?

- 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.

Intrauterine ball (IUB)

- Another advance is the intrauterine ball a **flexible, frameless device**, introduced using a narrow, **3.2mm inserter**.
- Out of 40,000 insertions across Europe, only **1.6%** have been **expelled**.
- There have been just 42 pregnancies
- An efficacy rate of **99.89%**.

Intrauterine ball



Description

Manufactured by OCON Medical Ltd, the Intrauterine Ball (IUB™) SCu300B MIDI is a copper intrauterine device (Cu-IUD) comprised of **copper beads** with a total exposed **copper surface of 300mm²** strung on a flexible Nitinol (nickel/titanium alloy), PET-coated frame.

Description

Once the IUB is released from the **3.2mm diameter insertion tube** into the uterus it coils into a **spherical shape** measuring **15mm** in diameter.

A monofilament **blue** polypropylene double tail **thread** is attached to one end of the IUB frame to aid detection and removal of the device.

Intrauterine ball

The SCu300B MIDI has been available in the UK since March **2017.**

The IUB also comes in 2 other sizes:

12 mm and **18 mm**,

which are not available in the UK.

Indication. Cost.

The IUB is indicated for intrauterine contraception for up to **5 years**.

Cost The unit price of the IUB is **£38**

(or £7.60/year for full 5 year use).

Intrauterine ball

- Interim data from a study of 336 patients showed slightly **less bleeding** from the ball compared to a traditional IUD.
- Up to two years post-insertion there was **significantly less pain**, but the full data has not yet been released.
- Theoretically less dysmenorrhoea
- Lacking safety and efficacy data

What is the evidence for safety and effectiveness of the IUB?

- Currently there are **no published safety** or effectiveness data from clinical trials of this specific model of the IUB.
- One small study which included 51 women using a 12mm IUB device (the SCu380A) suggested high expulsion rates of 27% (14/51) for that device at 12 months.
-

What is the evidence for safety and effectiveness of the IUB?

- On the basis of post-marketing surveillance data, the manufacturer suggests that the IUB appears to have a favourable safety profile and similar effectiveness to other currently available Cu IUDs.
- However, the FSRH CEU is unable to comment as to the reliability with which adverse events were reported for inclusion in this data set.

Conclusion

- The novel, spherical, flexible design of the SCu300B MIDI IUB has potential to **broaden contraceptive choice** for women seeking effective, hormone-free contraception;
- however **safety**, effectiveness and acceptability data from robust, independent studies and studies comparing the SCu300B MIDI with other Cu-IUD are **lacking**.
- The **CEU** will continue to monitor evidence relating to the IUB and provide an update when new evidence is published.

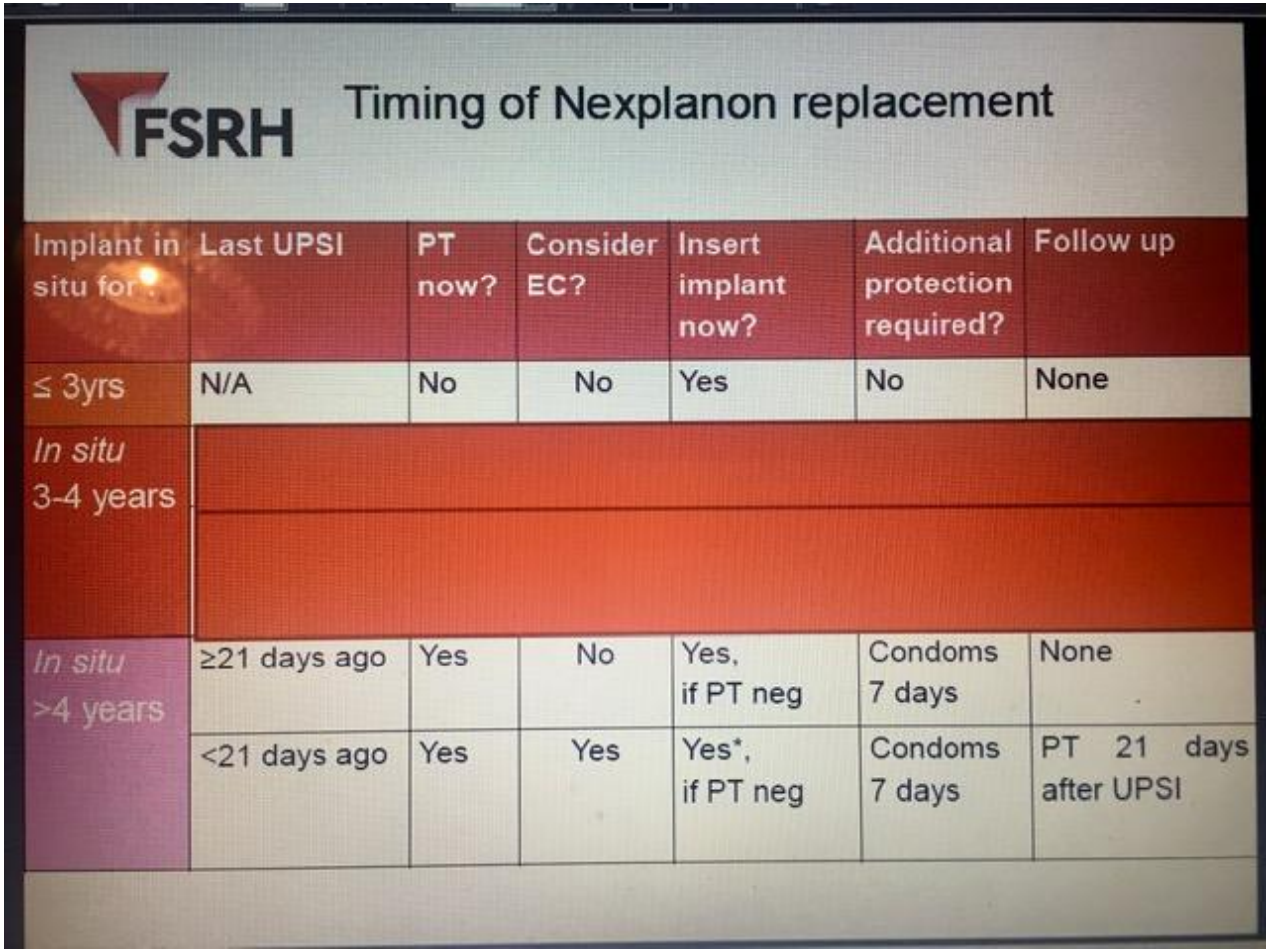
New in Nexplanon/SDI insertions

FSRH updates. What if an implant has recently expired?

Risk of pregnancy in the 4th year of use of the ENG-IMP appears to be low, although

evidence is as yet too limited to recommend 4 years of use as standard.

Timing of SDI/Nexpalnon replacement



FSRH

Timing of Nexplanon replacement

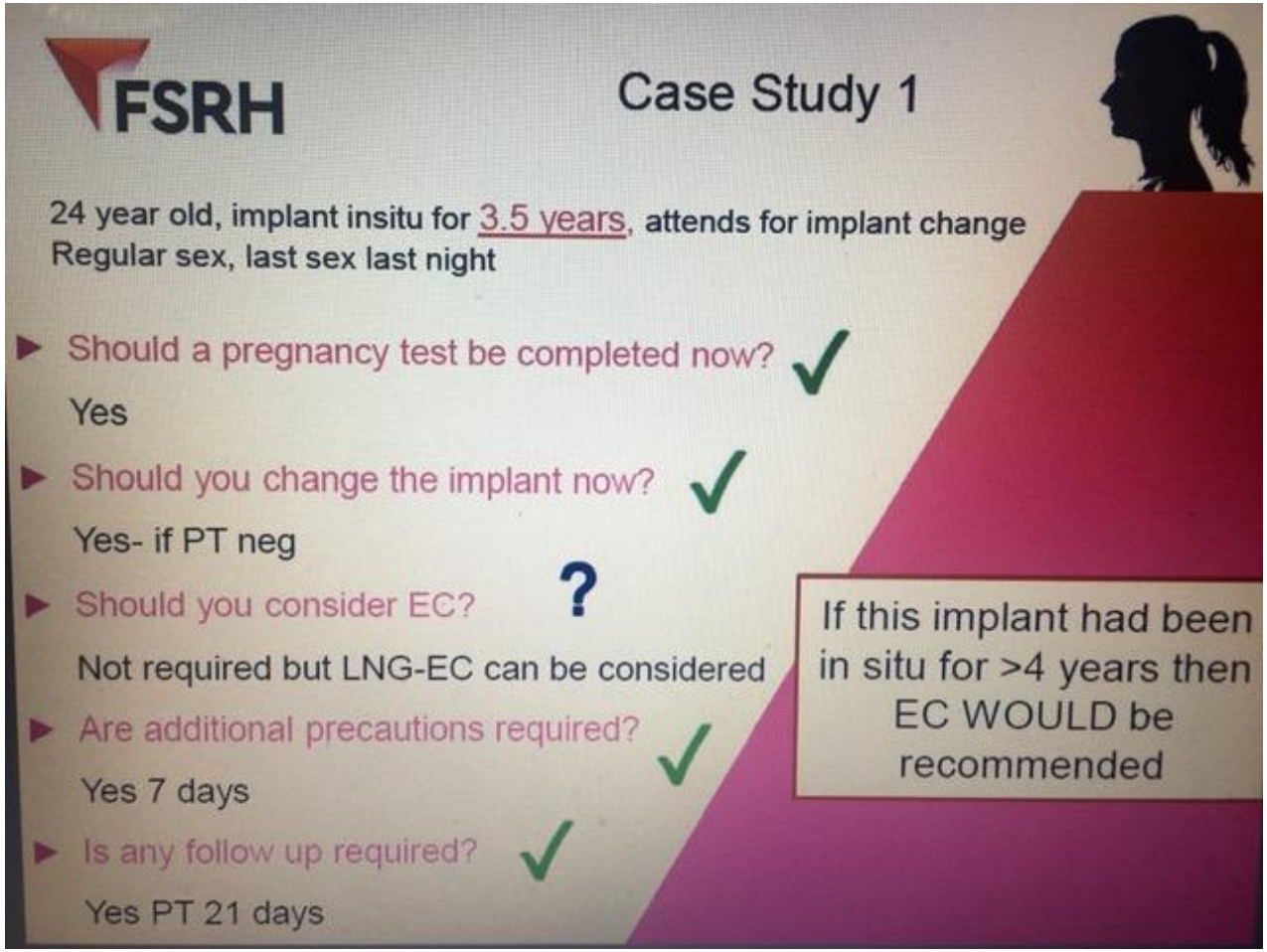
Implant in situ for:	Last UPSI	PT now?	Consider EC?	Insert implant now?	Additional protection required?	Follow up
≤ 3yrs	N/A	No	No	Yes	No	None
In situ 3-4 years						
In situ >4 years	≥21 days ago	Yes	No	Yes, if PT neg	Condoms 7 days	None
	<21 days ago	Yes	Yes	Yes*, if PT neg	Condoms 7 days	PT 21 days after UPSI

FSRH updates. What if an implant has recently expired?

- If an individual presents after UPSI in the 4th year of use of an ENG-IMP, emergency contraception is unlikely to be required;

- a new implant can be inserted immediately, with additional contraceptive precautions for 7 days.

Case study from FSRH



New on switching to another contraception /IUCD

- Comprehensive **switching table**
- Implant in situ for **3-4 years**:

➢ **Effectiveness** still likely to compare favourably with typical use of oral contraception

➢ **PT** negative today

➢ **Condoms** for next 7 days if IUS

➢ FU for **PT** in **3 wks** after last UPSI

SDI side effects update

- **Unpredictable bleeding** pattern
- **Insufficient evidence** to conclude or exclude causative association:

➢ headache

➢ weight change

➢ depression

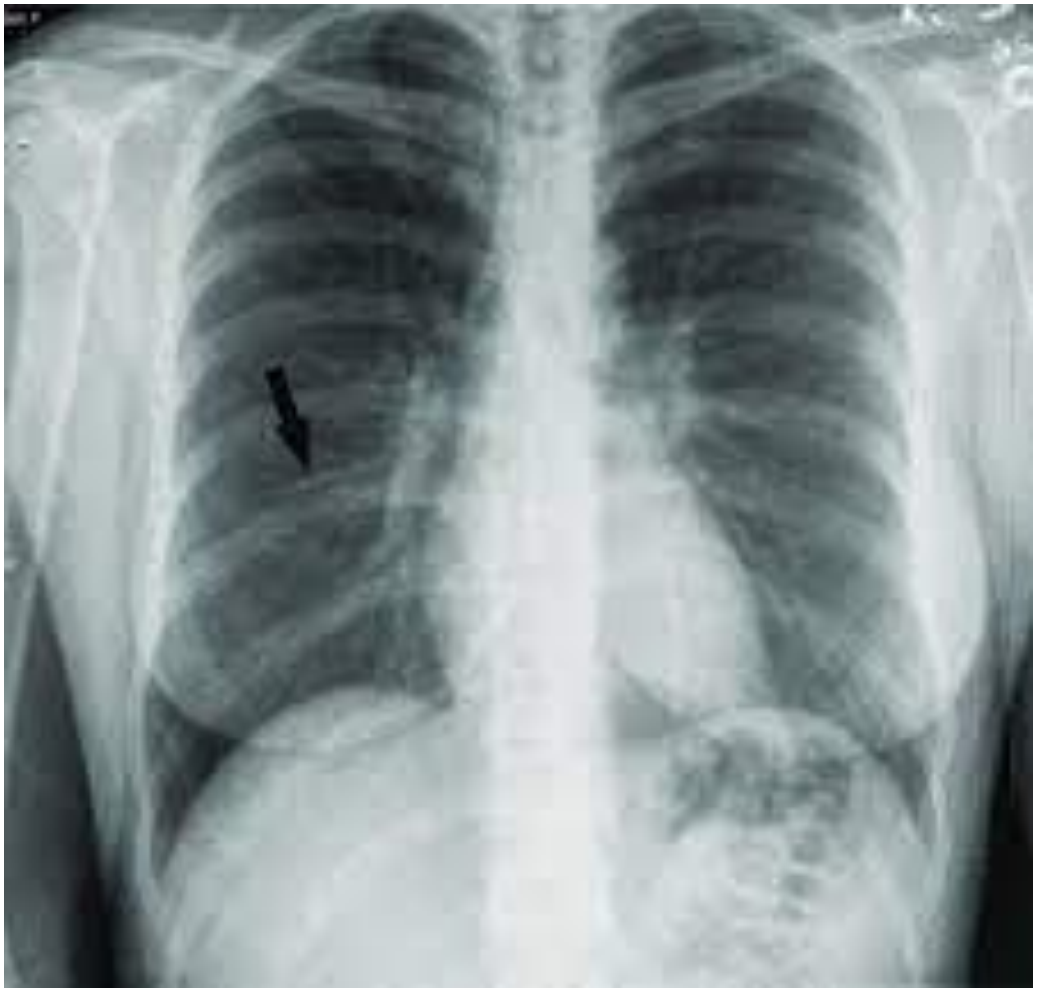
- **Acne** : new onset, worsening or improvement

SDI insertion updates

SDI insertion for individuals with **higher risk of bleeding:**

- To **avoid NSAID** for pain relief peri procedure
- If platelets >50- to do insertion
- If **platelets < 50** – to check with **haematologist**

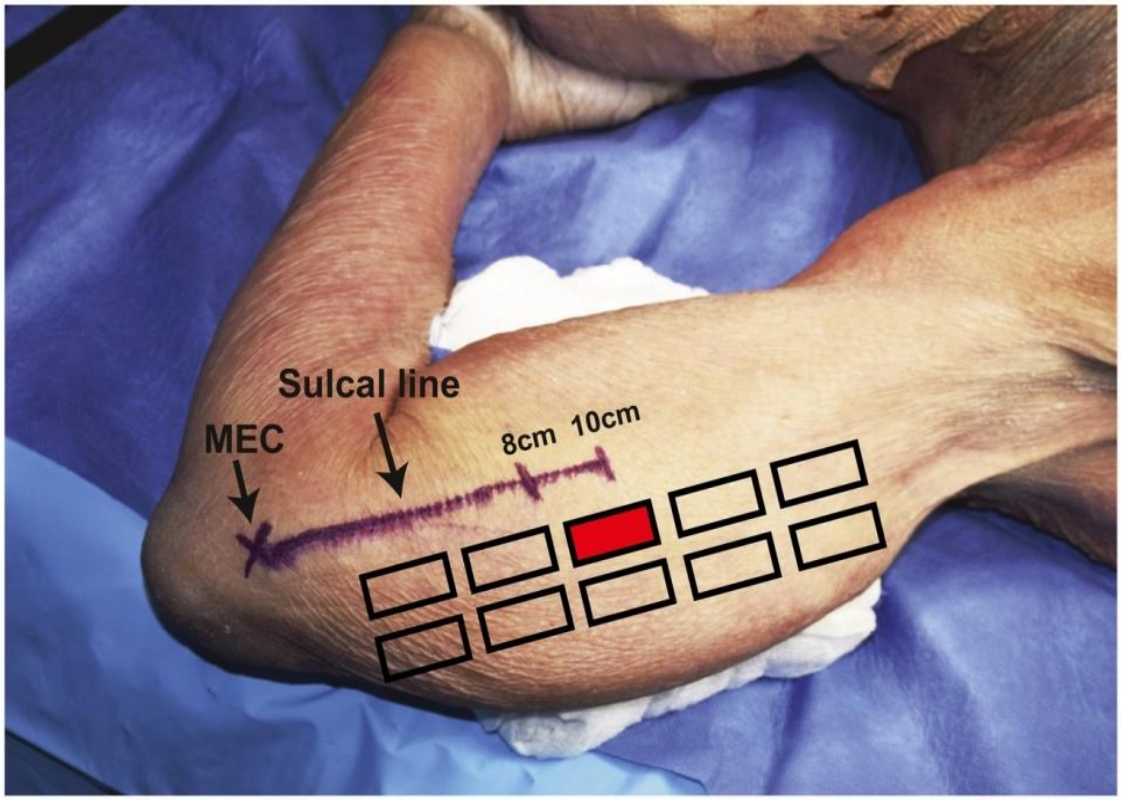
Risk of intravascular insertion and migration



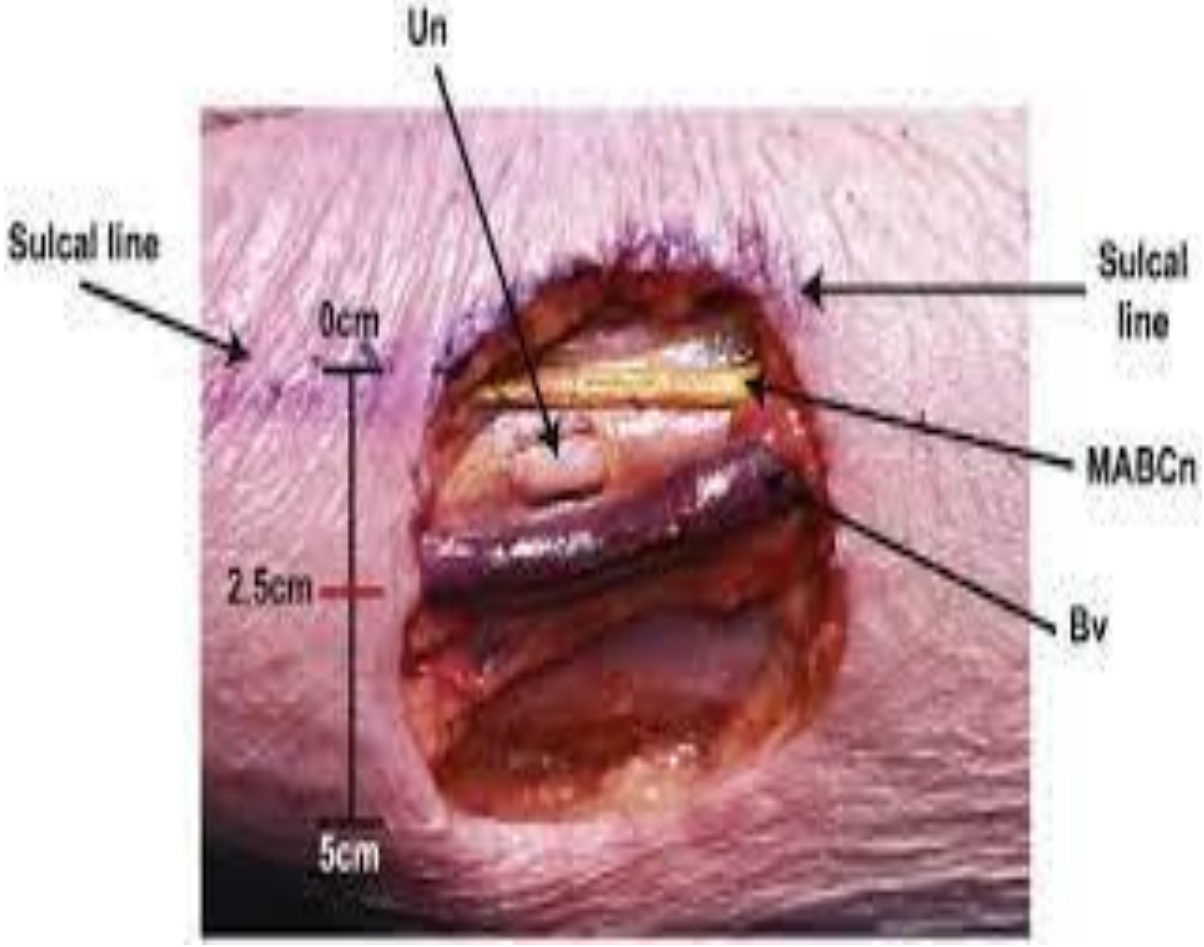
Risks of SDI insertions & removals

- Risk of **intravascular insertion** and **distant migration**
- Risk of **nerve damage** at time of insertion / removal

Cadaver study



Neuro-vascular structure at sulcal line



New insertion site

- FSRH recommendation for the new insertion site over triceps has aligned with **new manufactured guidance**

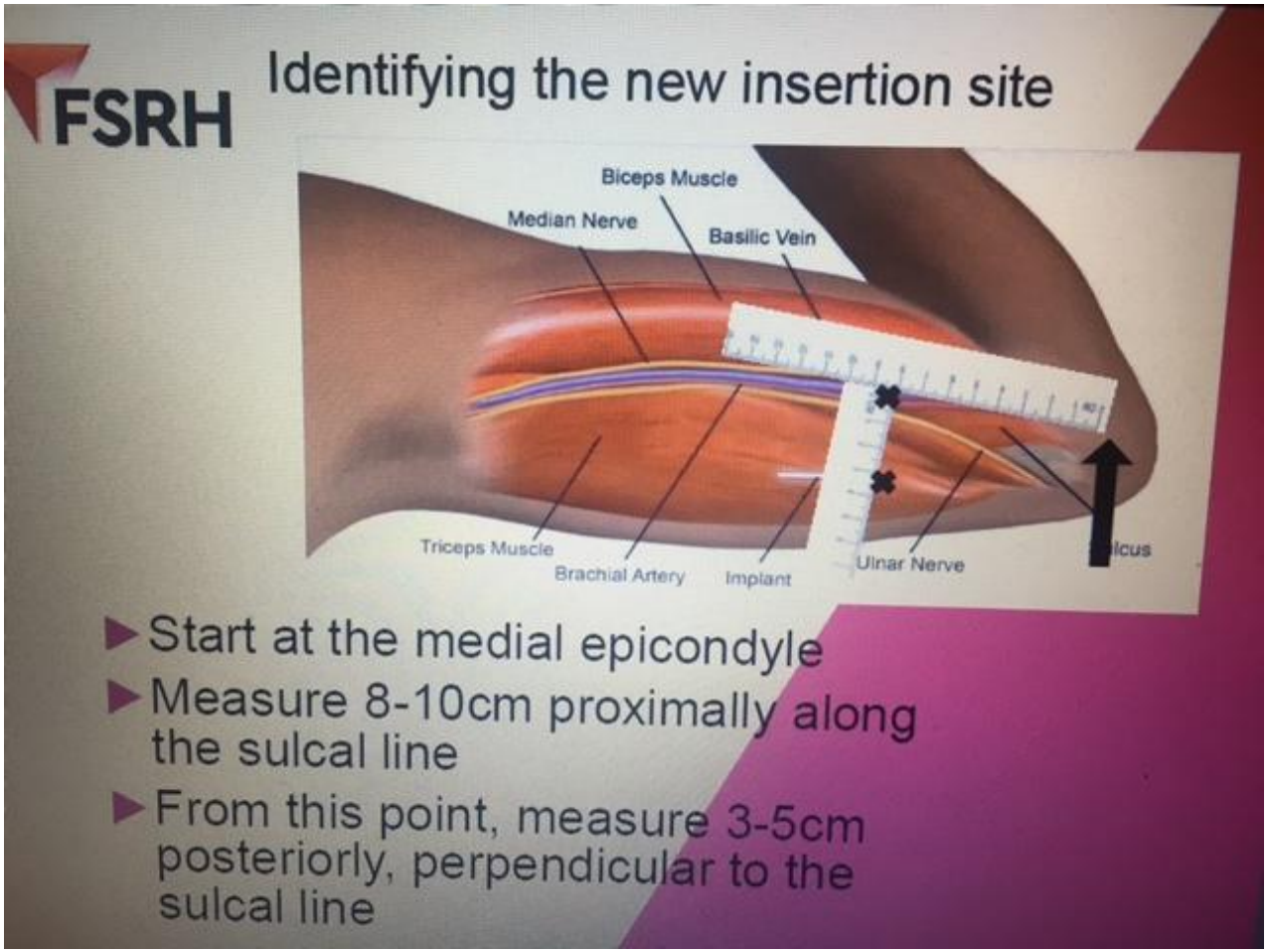
- Nexplanon **over triceps**

Insertion procedure key points

- The individual should lie on their back with their **arm abducted to 90°,**
- their **elbow flexed** and their hand behind their head.
- Local anaesthesia may be achieved with **lidocaine 1%** OR

  ethyl chloride spray

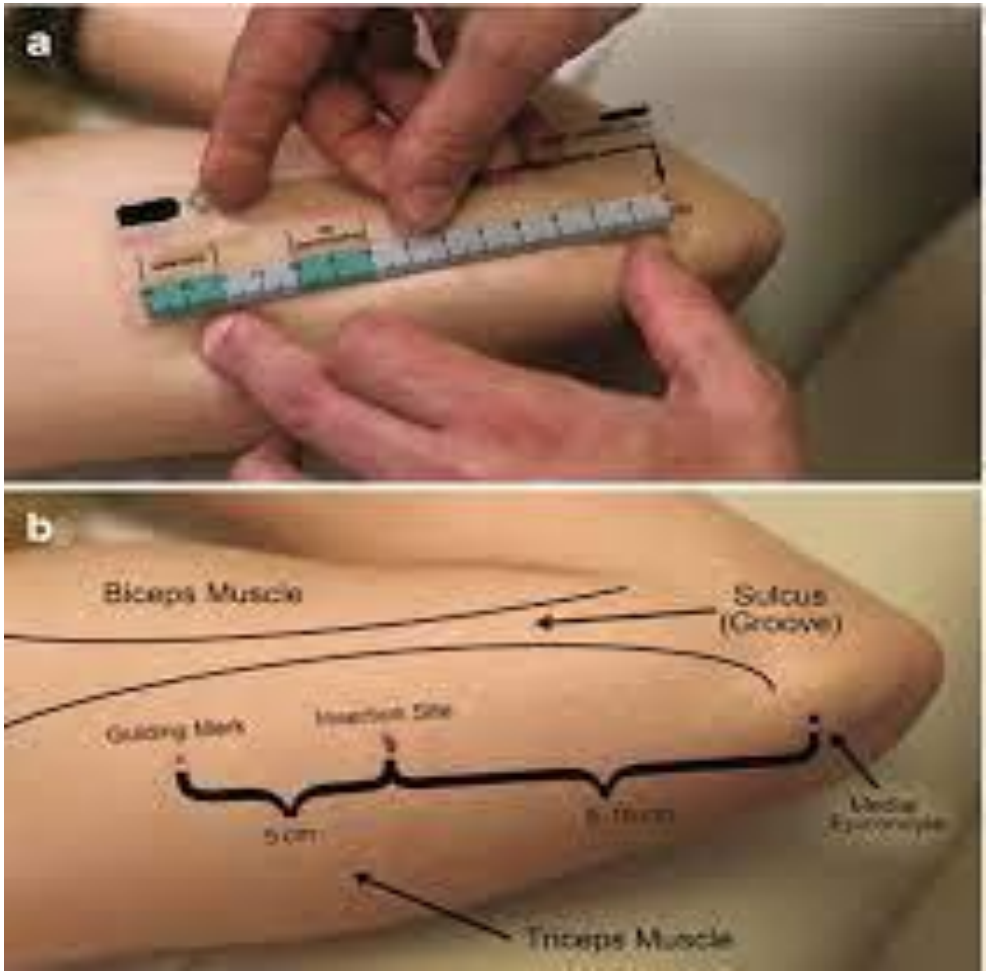
Identifying new insertion site



To identify the new insertion site:

- start at the **medial epicondyle** measure
- **8-10 cm** proximally along the sulcal line from this point,
- measure **3-5cm posteriorly** (over triceps), perpendicular to the sulcal line
- **pierce the cleansed skin** with the implant introducer at this point and
- advance the **introduction needle** proximally just under the skin, parallel to the sulcal line

New SDI insertion side

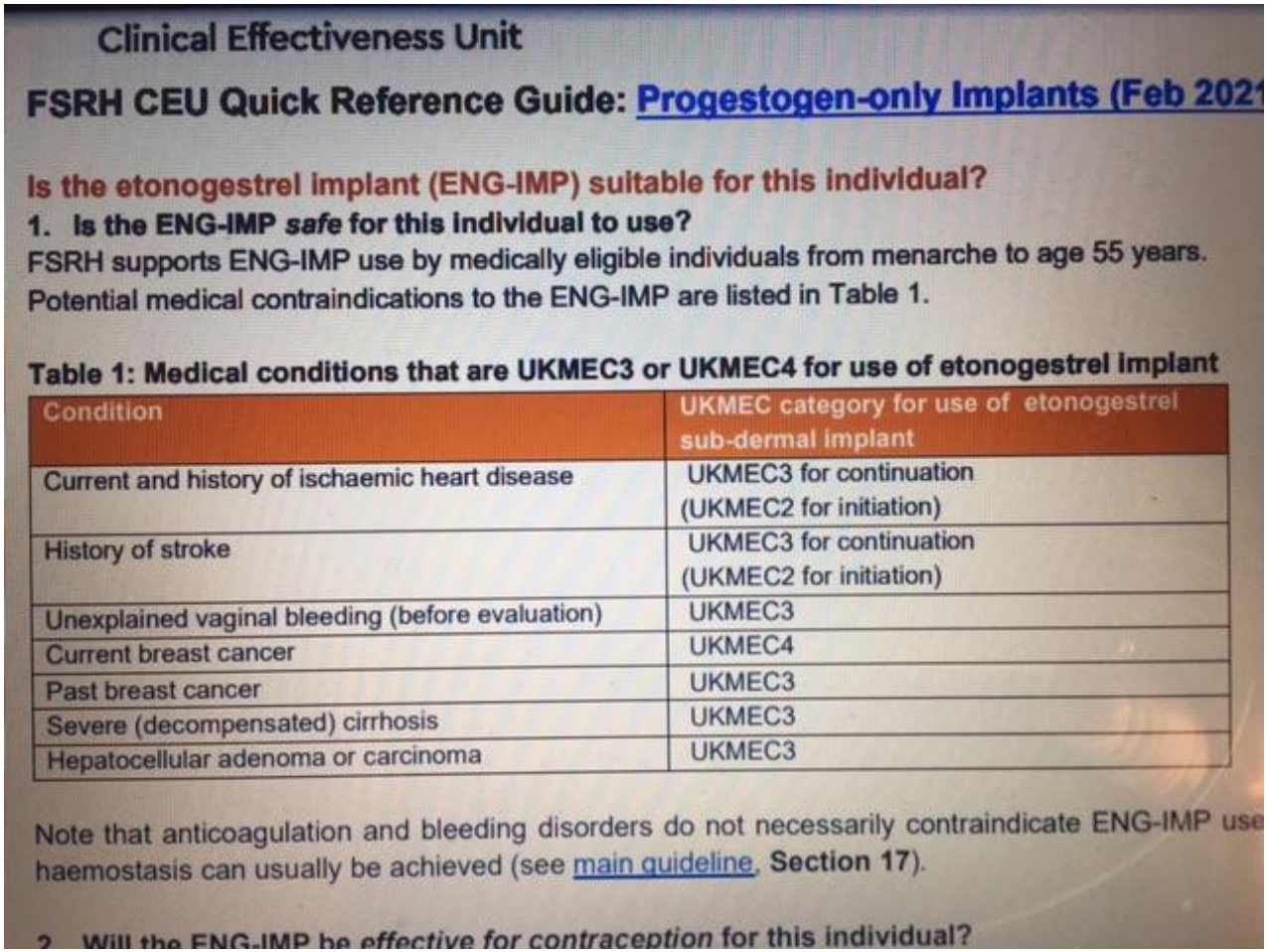


Nexplanon. High BMI

- High BMI > 35 : No pregnancy risk.

- With very high BMI- not enough study

UKMEC 3 & 4 for SDI



Clinical Effectiveness Unit

FSRH CEU Quick Reference Guide: Progestogen-only Implants (Feb 202

Is the etonogestrel implant (ENG-IMP) suitable for this individual?

1. Is the ENG-IMP *safe* for this individual to use?

FSRH supports ENG-IMP use by medically eligible individuals from menarche to age 55 years. Potential medical contraindications to the ENG-IMP are listed in Table 1.

Table 1: Medical conditions that are UKMEC3 or UKMEC4 for use of etonogestrel implant

Condition	UKMEC category for use of etonogestrel sub-dermal implant
Current and history of ischaemic heart disease	UKMEC3 for continuation (UKMEC2 for initiation)
History of stroke	UKMEC3 for continuation (UKMEC2 for initiation)
Unexplained vaginal bleeding (before evaluation)	UKMEC3
Current breast cancer	UKMEC4
Past breast cancer	UKMEC3
Severe (decompensated) cirrhosis	UKMEC3
Hepatocellular adenoma or carcinoma	UKMEC3

Note that anticoagulation and bleeding disorders do not necessarily contraindicate ENG-IMP use haemostasis can usually be achieved (see main guideline, **Section 17**).

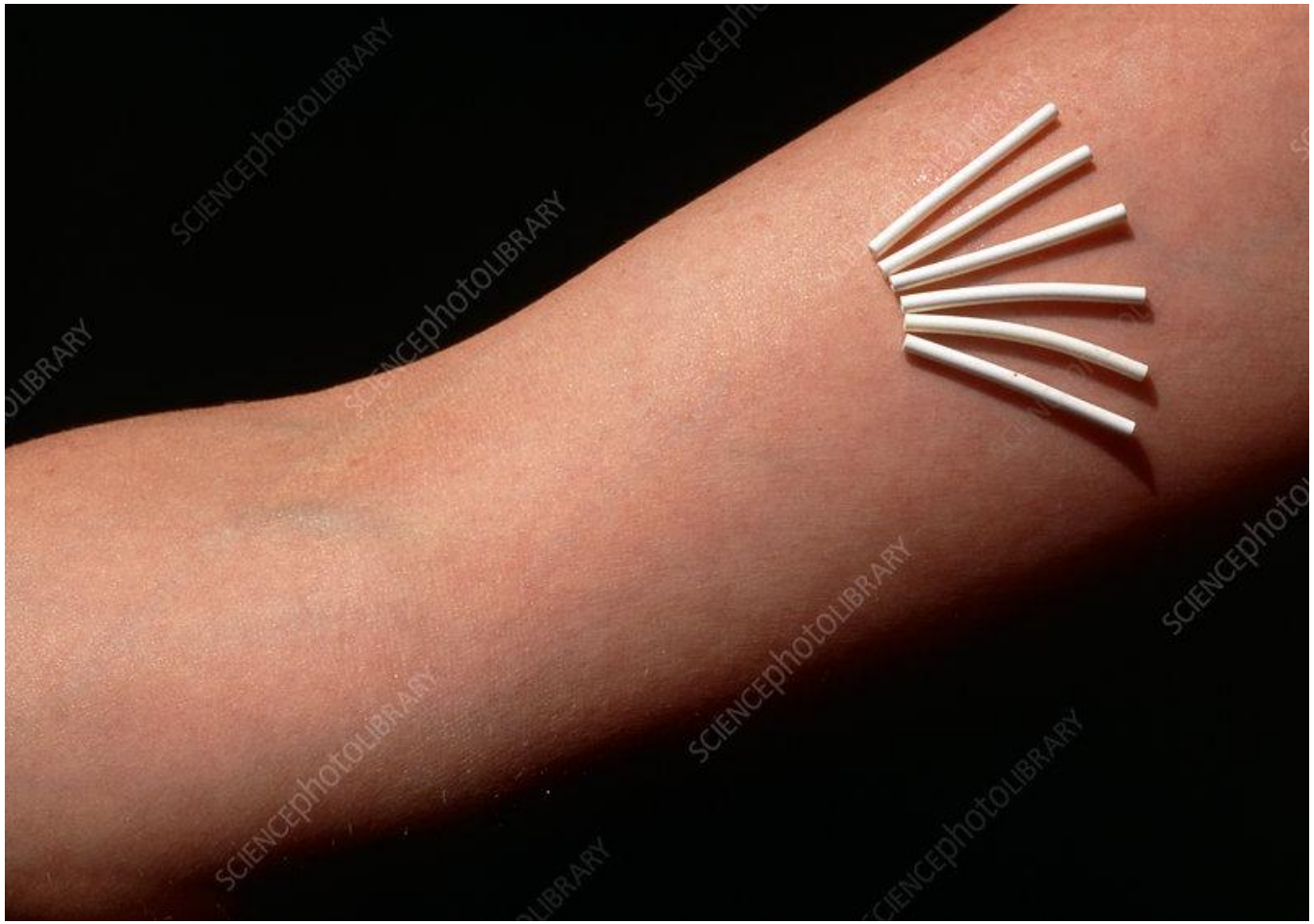
2. Will the ENG-IMP be *effective for contraception* for this individual?

Broken Implant

- Remove at the site of break sliver plasticated cover incision at site of break
- Don’t know efficacy of broken Implant

Jadelle: 2 rods LNG

Norplant: 6 rods



Take home messages about new in SDI

- The recommended **site** of SDI has changed
- **Intravascular migration** of Implant is uncommon, but exact frequency is unknown
- **Duration of use:**
- Extended use of Nexplanon during the pandemic is appropriate, but standard duration of use is still 3 years

Bone mineral density

- More caution with interpretation of evidence
- No longer able to say that definitely no effect impact on bone mineral density

Switching to IUC in 4th year of use

Less concerns a out switching to IUC in year 4

In the 4th year of Nexplanon use,

- if a **PT is negative** on the day,
- **IUC** can be inserted even if there has been **UPSI in the last 21 days**.
- **Condoms** are required **for 7 days** for an IUS and
- a **FU PT** is required.

Sayana press

- **Anaphylaxis**. None anaphylaxis
- Video link consultation
- Not in clinic, so theoretic risk
- **Adult present**
- **www.sayanaanswers.co.uk** send reminder
- Dent at site injection due to **lipoathrophy**
- Referral to **plastic surgery**

New COC ring

Syreniring

- Don’t need refrigerating

Syreniring

CHC

- Syreniring

NuvaRing

NuvaRing 0.12mg/0.015mg per day vaginal delivery system (Organon Pharma (UK) Ltd)

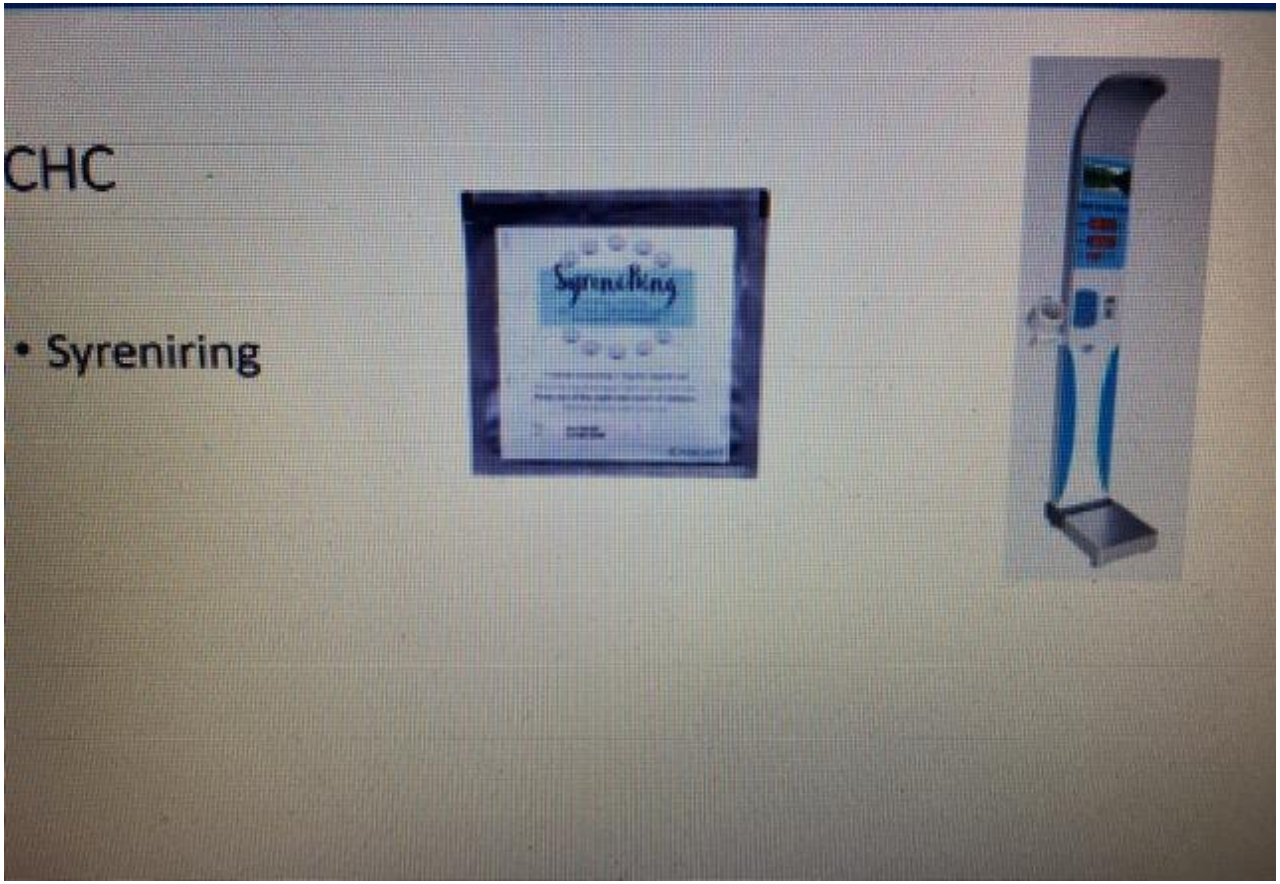
- Active ingredients
  - Ethinylestradiol 2.7 mg
  - Etonogestrel 11.7 mg
- 3 system (POM**) £29.70**

SyreniRing

SyreniRing 0.12mg/0.015mg per day vaginal delivery system (Crescent Pharma Ltd)

- Active ingredients
  - Ethinylestradiol 2.7 mg
  - Etonogestrel 11.7 mg
- 3 system (POM**) £23.76**

Auto calf for BP + BMI+ Ticket



COC for 1 year

- **Standard** regime **5** pack
- **Tailored** regime **5-6** pack

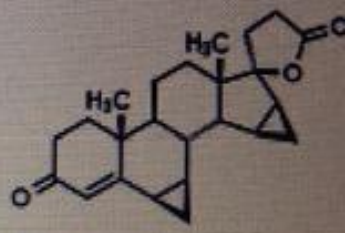
New POP: Drosperinone

- Licensed by FDA “Slynd”
- 4 mg DRSP
- **24/4 regimen**
- **Better bleeding pattern**, with placebo
- An ovulation
- Missed pills rules
- 30-34 hours life

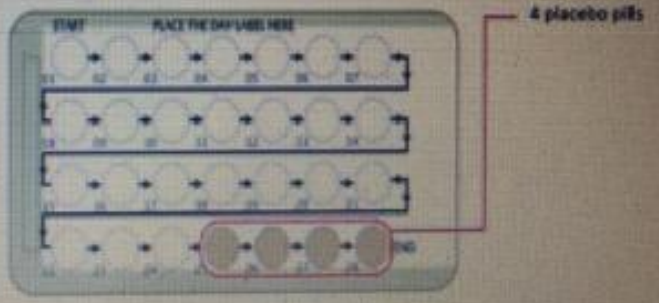
Drosperinone POP

Drospirenone POP

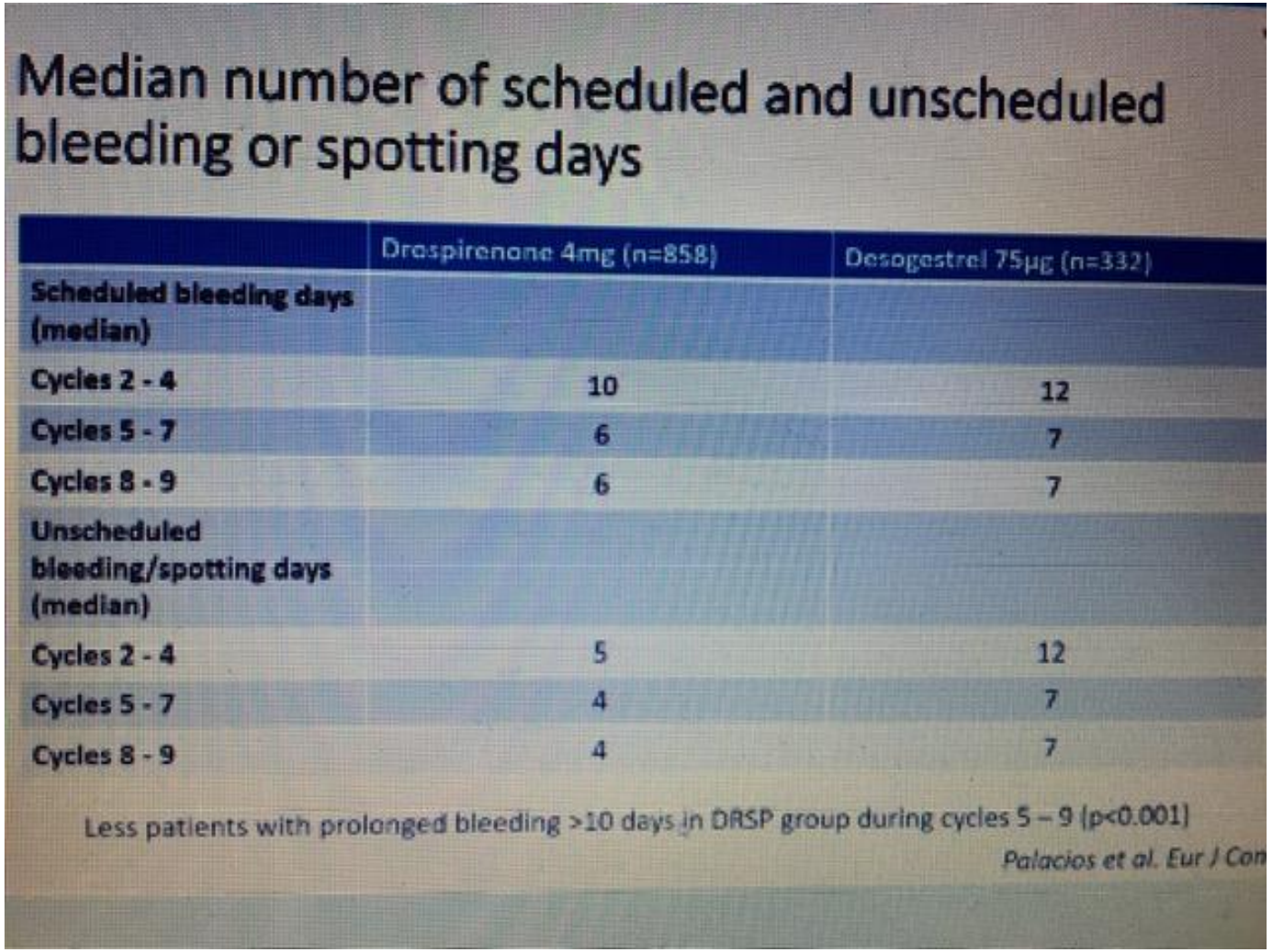
- Licenced by FDA 'Slynd'
- 4mg DRSP
- 24 / 4 regimen
- Similar efficacy to CHC
- Anovulatory
- Missed pill rules



Drospirenone



Drosperinone POP



Median number of scheduled and unscheduled bleeding or spotting days

	Drospirenone 4mg (n=858)	Desogestrel 75µg (n=332)
Scheduled bleeding days (median)		
Cycles 2 - 4	10	12
Cycles 5 - 7	6	7
Cycles 8 - 9	6	7
Unscheduled bleeding/spotting days (median)		
Cycles 2 - 4	5	12
Cycles 5 - 7	4	7
Cycles 8 - 9	4	7

Less patients with prolonged bleeding >10 days in DRSP group during cycles 5 – 9 ($p<0.001$)

Palacios et al. Eur J Con

Drosperinone POP

- Less scheduled and unscheduled bleeding on Drosperinone
- European Union countries since 2019
- If you **miss** one yellow pill: Take the pill as soon as possible and take the next pill at your regular schedule. If you **miss** two yellow pills in week 1 or 2: Take the two pills as soon as possible and the next two pills the next day. Continue taking one pill a day until you finish the pack.

Abx

- We don’t think that any problem with non enzyme induced
- 90% - effectiveness of COC

Non-enzyme inducing antibiotics and hormonal contraceptives

- FSRH CEU Statement: Response to Recent Publication Aronson and Ferner, 2020 “Analysis of reports of unintended pregnancies associated with the combined use of non-enzymeinducing antibiotics and hormonal contraceptives” 2 February 2021

What is the current guidance?

After systematically reviewing all published evidence on this topic, the US Center for Disease Control and Prevention , the WHO, and the FSRH CEU have concluded on multiple occasions (2009, 2010, 2015, 2017) that common **non-enzyme–inducing antibiotics DO NOT** impair the effectiveness of hormonal contraception, including COCs, patches, or rings and that extra precautions are not required when antibiotics are prescribed

How does this study affect FSRH guidance?

- Given its substantial limitations, the findings from the Aronson and Ferner (2020) study are not scientifically robust enough to warrant any change to FSRH CEU guidance.
- FSRH CEU guidance remains that additional contraceptive precautions are not required when antibiotics are prescribed to users of hormonal contraception .
- In women using **known enzyme-inducing medications** long-term, including enzyme inducing antibiotics, the FSRH CEU recommends **IUC** or injectable contraception (**DMPA**).

FSRH CEU Statement: Contraception for Women with Eating Disorders

- Key Points Sexually active women of reproductive age with eating disorders require effective contraception despite the fact that amenorrhoea and anovulation are common in this population.
- Women with an eating disorder who are underweight should be advised of the increased risk of adverse pregnancy outcomes when underweight and should be advised to delay conception until the condition is in remission.

Contraception for Women with Eating Disorders

- **LARC** methods remain the most effective methods of contraception in this population.
- Although **combined hormonal contraceptives** are commonly used to provide ***bone protection***, they have not been shown to protect bone mineral density in women with anorexia.

Silicone ring

- A significant development, aimed at low income countries is **Annovera**, approved in August 2018 by the FDA.
- A combined hormonal contraceptive (CHC) in a soft, flexible ring made of silicone, it delivers serum levels of **15mcg ethinyl estradiol (EE) and 150mcg nesterone.**

Silicone ring

- It is inserted for three weeks, removed for one, and **used for 13 cycles**.
- A Phase 3 study of more than 2,000 women at 27 sites in the USA, Latin America, Europe, and Australia found efficacy and safety similar to other CHCs, while there was no increased risk of vaginal infection and **no need for refrigeration.**

Wireless microchip

- The first wirelessly-controlled drug delivery microchip has been developed in research backed by the Gates Foundation. It is ‘the size of a scrabble tile’, just 2cm by 2cm, and less than 1mm deep, said Dr Haider. It can be implanted subcutaneously into the buttock, abdomen or upper arm.

Wireless microchip

- Pre-clinical testing started in 2016 and it is set to be available soon. It supplies **30mcg levonorgestrel daily**, from a sealed array of micro-reservoirs, for **up to 16 years**.
- Activated by a key fob, it can be controlled remotely.
- However, the fob has to be held over the implant, to ensure the right patient is being targeted.

Vaginal rings (Annovera™)

User-controlled methods such as vaginal rings have become popular.

A novel contraceptive vaginal system (Annovera™) for **1-year of use** is expected to become available in the US by the end of the year.

Future contraception methods

- Still in an early stage of research are contraceptive methods **for 1-month** or
- **on-demand use**, and
- **biodegradable implants** and
- **microneedles**, all easier to administer.

Male hormonal contraception (MHC)

Many men are willing to share responsibility for family planning.

Their choices are limited to

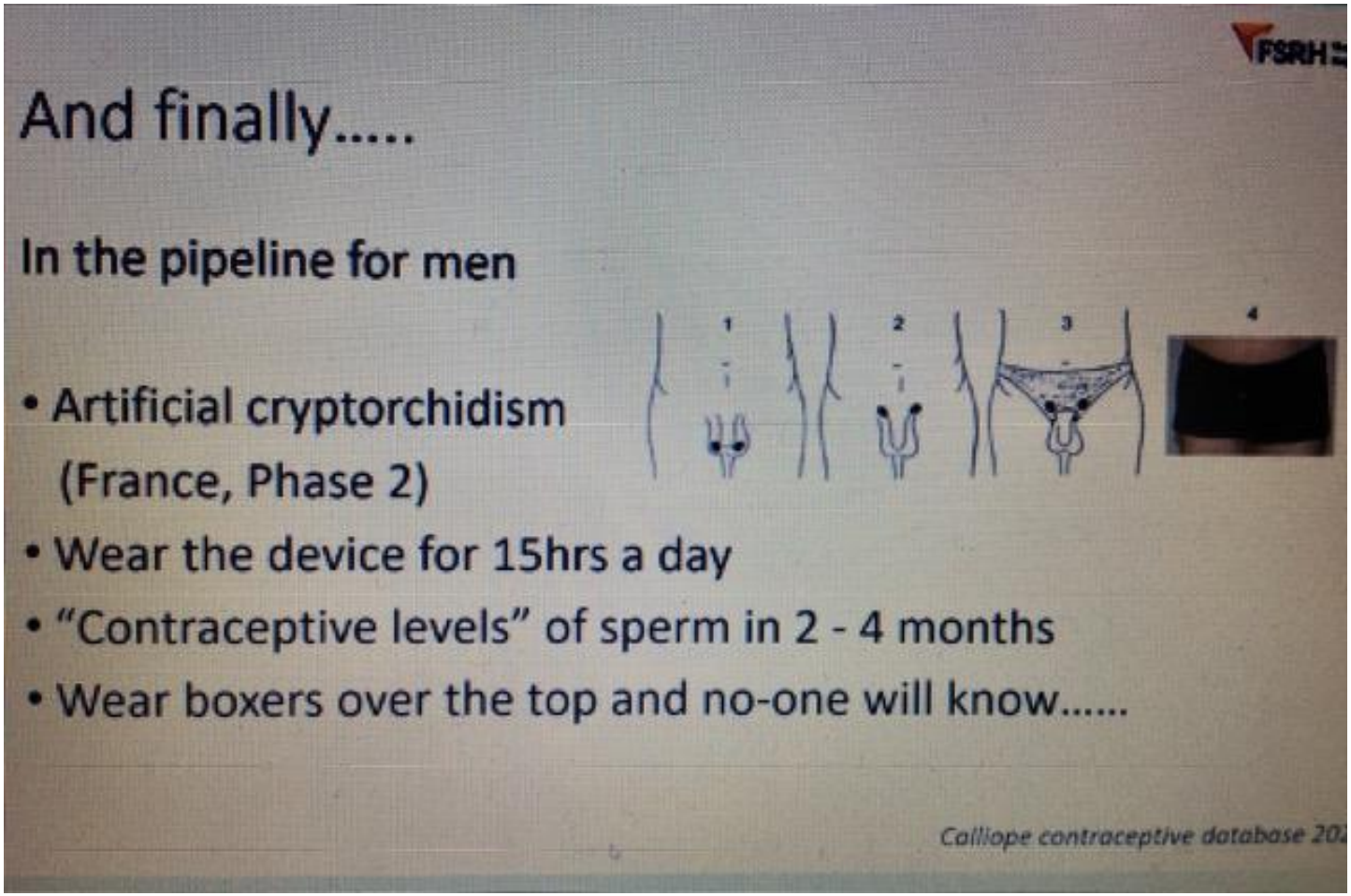
- condom,
- withdrawal and
- male sterilization, which are not popular.

Male hormonal contraception (MHC)

Increasing options and services for men, addressing their concerns and dispelling myths will increase male engagement.

The most advanced MHC currently in development is a **transdermal gel** effective in suppressing spermatogenesis while maintaining male habitus.

Male contraception



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Thank you!