

Managing problematic bleeding with HRT

**Northern Cancer Alliance NHS Foundation Trust
Meeting 12.30pm on 11 December 2025**

Dr Diana Mansour
Consultant in Community Gynaecology,
Newcastle upon Tyne, UK

Meet the speaker – Dr Diana Mansour



**Consultant Gynaecologist, Newcastle upon Tyne
Visiting Professor, University of Sunderland
Clinical appraiser for Newcastle Hospitals**

Previous Associate Clinical Lecturer at Newcastle University

Previous Senior Vice President at the College of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists

Member of the CoSRH UKMEC steering group and guidelines group

Accredited BMS Specialist

First author to over 100 peer-reviewed publications

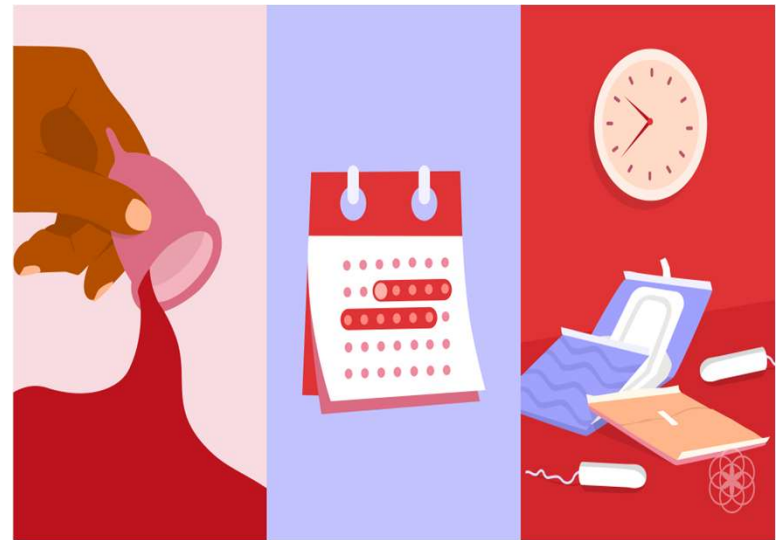
Co-wrote 'Contraception Made Easy' textbook for primary care

How to manage bleeding problems with HRT?

Learning objectives

By the end of this talk, you should be able to.....

- Describe what is meant by unscheduled bleeding with HRT
- Know when to investigate and when to refer
- Modify HRT regimens to improve bleeding patterns



Management of unscheduled bleeding on hormone replacement therapy (HRT)

The British Menopause Society (BMS) is the specialist authority for menopause and post reproductive health in the UK. The BMS educates, informs and guides healthcare professionals, working in both primary and secondary care, on menopause and all aspects of post reproductive health.

BMS guidelines, prepared by the BMS medical advisory council in partnership with other specialist organisations and Royal Colleges, address key disorders and controversial topics relating to menopause and post reproductive health. They reflect new studies together with recent medical and scientific information from articles in professional journals, plus informal consensus.

The guidelines are evidence-based, comprehensively referenced and peer reviewed and they are regularly updated.

Definition of unscheduled bleeding with HRT

- **Unscheduled bleeding on HRT is.....**
 - Irregular bleeding occurring after initiating/changing continuous combined HRT (ccHRT)
 - **Or** in addition to scheduled withdrawal bleed in sequential HRT(sHRT)
- **Unscheduled bleeding is common**
 - within first 6 months of initiating either sHRT or ccHRT
 - **Or** within 3 months of change in dose/preparation in those already established on HRT
- **It occurs in up to 38% of sHRT users and 41% using ccHRT**
 - More common in users of transdermal HRT compared to oral HRT
 - More common in those of high dose HRT

Helping women navigate their menopause is a significant part of a GP's workload

Around one third of the female population in the UK, an estimated 13 million, is perimenopausal or menopausal

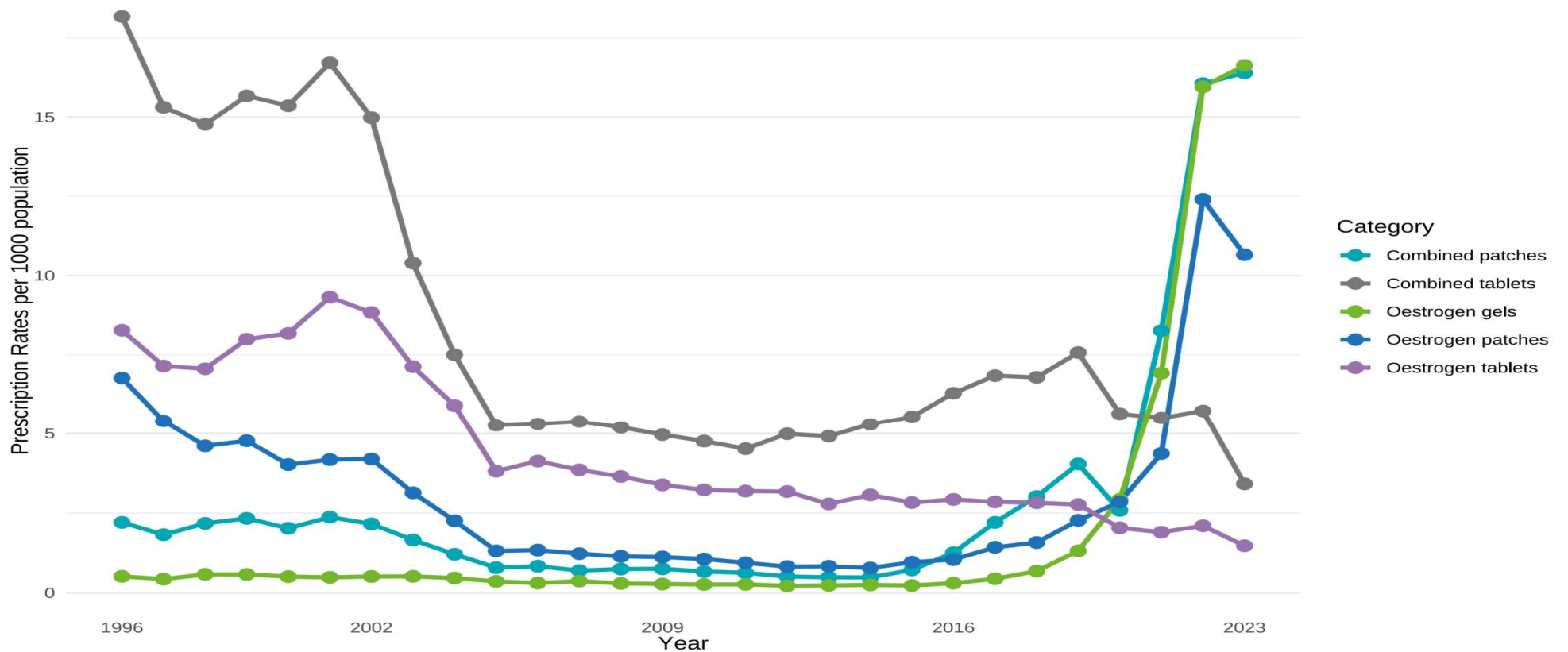


shutterstock.com · 2641869169

<https://www.medscape.co.uk/viewarticle/are-nices-menopause-updates-enough-2024a1000lfg>

Hormone Replacement Therapy Uptake and Discontinuation Trends from 1996-2023: an Observational Study of the Welsh Population

HRT Prescribing Rates by Type



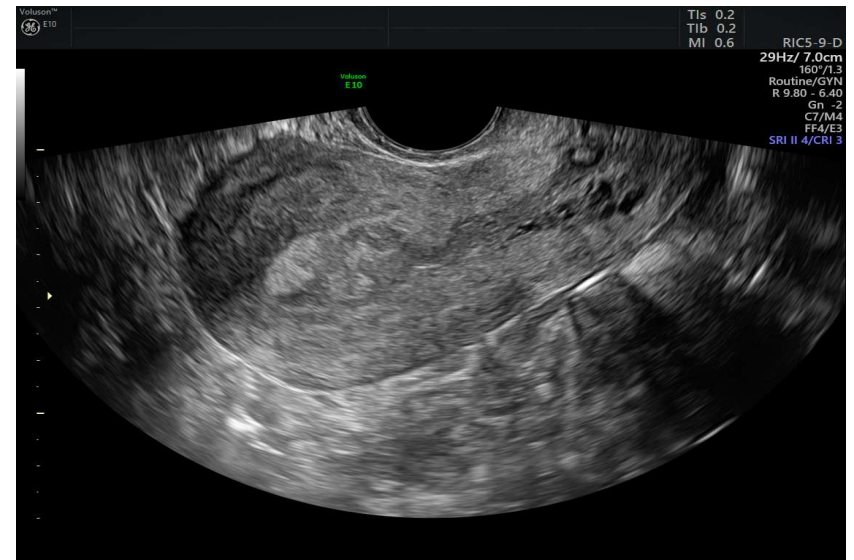
Huge increase in referrals for women with unscheduled bleeding with HRT

- **In England, 35% increased HRT use in 2021/2022 from previous year**
 - Estradiol gel and micronized progesterone - top two HRT products prescribed in 2022
 - Total number of people prescribed micronized progesterone increasing by 125%
- **43% increase in referrals for unscheduled bleeding to the Urgent Suspicion of Cancer Pathway over last 3 years**
 - Diagnosis from these referral rose by 2% over same time interval



Postmenopausal bleeding, HRT and endometrial cancer – a systematic review

- Systematic review 129 studies
- Pooled risk of endometrial cancer among women with PMB
 - 9% (95% CI, 8%-11%)

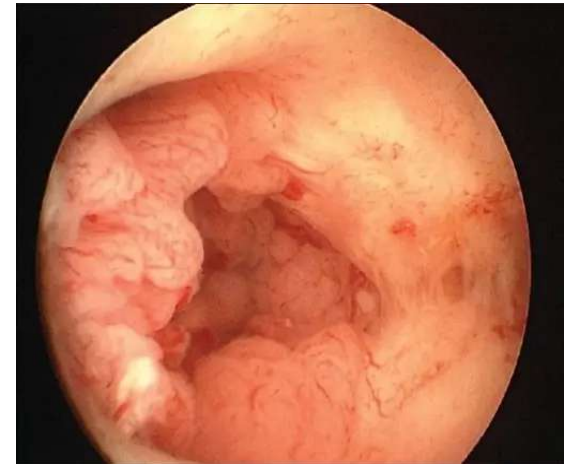


Clark et al JAMA Int Med 2018

Risk of endometrial cancer in postmenopausal women - UK data (Sheffield)

- **Of 1363 women with PMB under age 60**
 - 25 of 1124 non-users diagnosed with endometrial cancer
 - Cancer detection rate 2.18% (p value 0.0156)
- **214 women using HRT had PMB**
 - 1 had endometrial cancer (had used HRT >20 years)
 - Cancer detection rate 0.47% (about the same as background rate)
 - 1 Borderline 1A serous ovarian tumour
 - 3 Endometrial hyperplasia without atypia – 1.4%

Buchanan et al Post Reprod Med 2022



Assessment of women presenting with unscheduled bleeding on HRT

- **Clinical assessment**
 - Detailing bleeding patterns before and during taking HRT
 - HRT preparations used/for how long
 - Drug interactions
 - Individual risk factors for cancer
- **Offer an examination (abdominal, pelvic) and, where relevant**
 - Initial investigations such as cervical screening, STI screen and body-mass index (BMI)



Drug interactions

- **Dual action of Mounjaro (tirzepatide) can interact with oral HRT**
 - by reducing its absorption
- **Potentially making it less effective at protecting the endometrium**
- **Switching to non-oral HRT is safest approach**
 - Transdermal options plus 52mg LNG IUD or vaginal micronized progesterone
 - HRT patches containing progestogen
- **Increase oral progestogen dose (less preferred)**
 - Temporary increase oral progestogen dose
 - Uncertainty about absorption (published data)

once weekly
mounjaro[™]
(tirzepatide) injection



5 mg
0.6ml

Endometrial cancer risk factors in women taking HRT

- Risk factors for endometrial hyperplasia and cancer, independent of HRT, should be identified
- Major risk factors
 - BMI \geq 40
 - Hereditary conditions such as Lynch or Cowden syndrome
- Minor risk factors
 - BMI 30-39
 - Diabetes
 - Polycystic ovarian syndrome (PCOS)



MAJOR risk factors for endometrial cancer

- BMI \geq 40
- Genetic predisposition (Lynch / Cowden syndrome)
- Estrogen-only HRT for $>$ 6 months in women with a uterus
- Tricycling HRT (quarterly progestogen) for $>$ 12 months
- Prolonged sHRT regimen: use for more than 5 years when started in women aged \geq 45
- 12 months or more of using norethisterone or medroxyprogesterone acetate for $<$ 10 days / month or, micronised progesterone for $<$ 12 days / month, as part of a sequential regimen

MINOR risk factors for endometrial cancer

- BMI 30-39
- Unopposed estrogen > 3 months but < 6 months
- Tricycling HRT (quarterly progestogen) for > 6 but < 12 months
- > 6 months but < 12 months of using norethisterone or medroxyprogesterone acetate for < 10 days / month or, micronised progesterone for < 12 days / month, as part of a sequential regimen
- Where the progestogen dose is not in proportion to the estrogen dose for > 12 months (including expired 52 mg LNG-IUD)
- Anovulatory cycles, such as in Polycystic ovarian syndrome
- Diabetes

Use of progestogens in HRT to protect the endometrium

- **In women using sequential HRT (sHRT)**
 - offer a **minimum of 10 days** norethisterone (NET) or medroxyprogesterone acetate (MPA)
 - or **12 days of micronised progesterone**, per month
- **Women taking a sequential preparation (sHRT) over the age of 45 should be offered cHRT**
 - after five years of use
 - or by age 54 (whichever comes first)

Fixed dose estrogen and progestogen combinations vs separate dosing of oestrogen and progestogen

- Risk of endometrial cancer in the EPIC (European Prospective Investigation into Cancer and Nutrition) population in comparison with never users of HRT

Sequential combined HRT group vs HRT naive group HR: 1.41 95% CI: 1.08-1.83	Continuous combined HRT compared to non-users HR: 0.24 95% CI: 0.08-0.77
Subset of cases with separate oestradiol + micronised progesterone HR: 2.42 95% CI: 1.53-3.83	Tibolone compared to non-users HR: 2.96 95% CI: 1.67, 5.26

- A possible explanation is that there was less compliance in oestradiol (transdermal)/micronised progesterone (oral) users because there were two separate components to their HRT which had to be complied with

Key: Prescribed estrogen dose for ultra-low, low, standard, moderate and high dose regimens

	Ultra-low dose	Low Dose	Standard dose	Moderate dose	High dose
Oestrogel	½ pump	1 pump	2 pumps	3 pumps	4 pumps
Sandrena	0.25 mg	0.5 mg	1 mg	1.5-2 mg	3 mg*
Lenzetto spray	1 spray	2 sprays	3 sprays	4-5 sprays*	6 sprays*
Patch	12.5 µg	25 µg	50 µg	75 µg	100 µg
Oral estradiol	0.5 mg	1 mg	2 mg	3 mg [^]	4 mg [^]

* Off-license use
mg = milligrams

[^] Off-license use – rarely required to achieve symptom control
µg = micrograms

Endometrial cancer risk factors in women taking HRT

Estrogen dose	Micronised Progesterone		Medroxy progesterone		Norethisterone		LNG-IUD (52mg)	Dydrogesterone	
	continuous	sequential	continuous	sequential	continuous	sequential		Continuous	sequential
Ultra/Low	100 mg	200 mg	2.5 mg	10 mg	5 mg*	5 mg*	One – for up to 5 years of use	5mg	10mg
Standard	100 mg	200 mg	2.5-5 mg	10 mg	5 mg*	5 mg*		5mg	10mg
Moderate	100 mg	200 mg	5 mg	10 mg	5 mg	5 mg		5mg	10mg
High	200 mg	300 mg	10 mg [^]	20 mg [^]	5 mg	5 mg		10mg	20mg

* 1 mg provides endometrial protection for ultra-low to standard dose estrogen but the lowest stand-alone dose currently available in the UK is 5 mg (off-license use of three noriday POP i.e 1.05 mg, could be considered if 5 mg is not tolerated).

[^] There is limited evidence in relation to optimal MPA dose with high dose estrogen; the advised dose is based on studies reporting 10 mg providing protection with up to moderate dose estrogen.

In the absence of any risk factors for endometrial cancer

- **If unscheduled bleeding occurring within 6 months of starting HRT**
- **Or within 3 months after a change in HRT dose/preparation**
 - No further investigation needed
 - Offer adjustment in progestogen or HRT preparation for 6 months **in total**



In the absence of risk factors for endometrial cancer

- **If unscheduled bleeding continues in low-risk women, after 6 months of progestogen/HRT adjustments**
- **Discuss**
 - Urgent ultrasound (within six weeks)
 - Versus weaning off/stopping HRT and consideration of non-hormonal alternatives (to avoid invasive investigations)



For those women who elect to stop HRT

- **If bleeding settled at 4-week follow-up, and continued cessation of HRT is acceptable**
 - no further investigations are required
- **If irregular/prolonged bleeding continues at 4-week follow-up, when HRT has been discontinued**
 - Urgent suspicion of cancer pathway



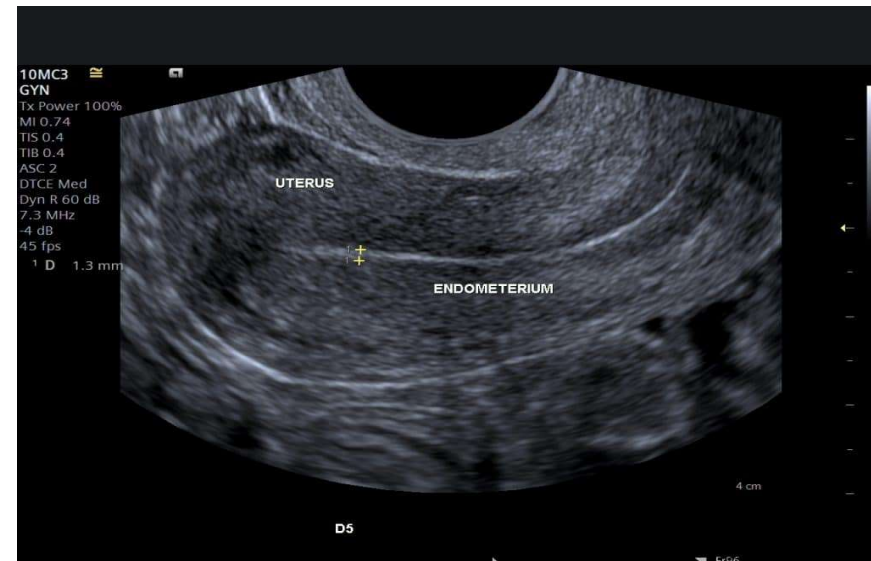
For those women who elect to stop HRT

- **If bleeding settled at 4 weeks and she wants to restart HRT**
 - Offer adjustments in progestogen/ regimen for 6 months
- **Arrange urgent TVS ultrasound**
 - if bleeding is heavy / persistent during this 6 months or restarts after this interval



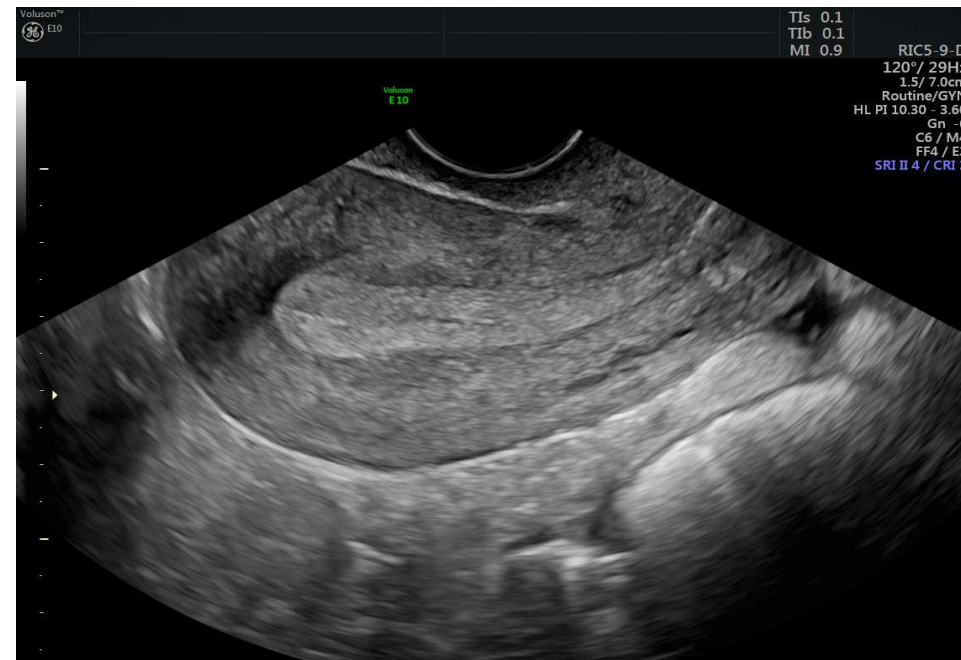
When to offer an urgent TVS (within 6 weeks)

- **Offer an urgent TVS within 6 weeks**
 - If the first presentation with bleeding occurs more than 6 months after initiating HRT
 - Or more than 3 months after changing/adjusting the HRT preparation
- **Offer an urgent TVS irrespective of interval since starting/changing HRT preparations**
 - If bleeding is prolonged / heavy
 - Or there are 2 minor risk factors for endometrial cancer



When to offer an 'urgent suspicion of cancer pathway' referral

- **Offer an 'urgent suspicion of cancer pathway referral'**
 - With 1 major or 3 minor endometrial cancer risk factors
 - Irrespective of bleeding type or interval since starting or changing HRT preparations
- **Adjustments to the progestogen, or stopping HRT**
 - should be offered whilst awaiting assessment



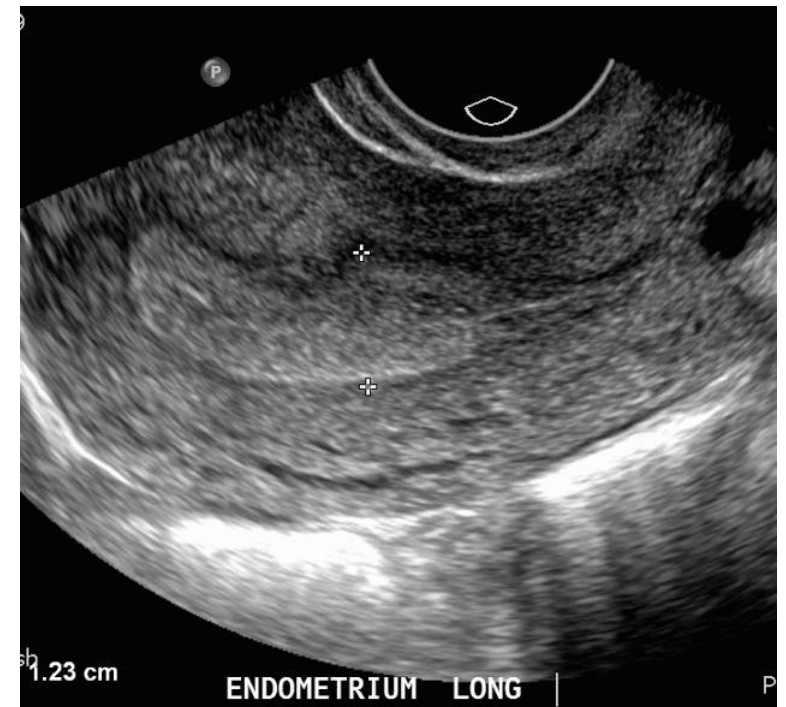
Findings from the transvaginal ultrasound scan (TVS)

- **Women with unscheduled bleeding, in the presence of a uniform endometrium (fully visualized)**
 - measuring ≤ 4 mm with ccHRT or ≤ 7 mm with sHRT
 - can be reassured that risk of endometrial cancer is low
- **Offer progestogen/HRT adjustments for 6 months**
 - Offer endometrial assessment on urgent pathway, if bleeding increases during these 6 months or continues after this interval



Findings from the transvaginal ultrasound scan (TVS)

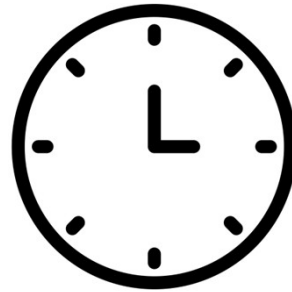
- **Women with a thickened endometrium on TVS (> 4 mm for ccHRT or > 7 mm for sHRT)**
 - should be offered referral to the urgent suspicion of cancer pathway for endometrial assessment (biopsy and/or hysteroscopy)



When to switch from sequential to continuous?

1 year +

After a minimum of 1 year of HRT, women who wish to avoid a monthly withdrawal bleed may attempt a switch to ccHRT– **to minimise the risk of endometrial hyperplasia.**



The timing of switching from sequential to continuous combined HRT should be considered in relation to the **woman's age and the frequency of her menstrual cycles (prior to commencing HRT).**

<50

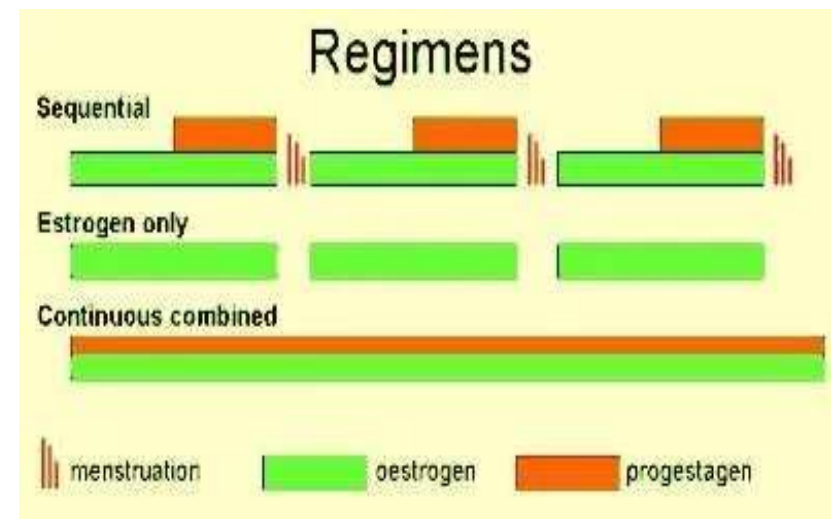
Women under 50 with shorter durations of amenorrhoea before starting HRT are likely to need to continue sHRT for longer duration before switching to ccHRT.

HRT, hormone replacement therapy.

Reference: 1. BMS Progestogens and endometrial protection; Accessed July 2025 [14-BMS-TfC-Progestogens-and-endometrial-protection-APR2023-A.pdf](#)

Managing unscheduled bleeding with sequential HRT (sHRT)

- **Desogestrel can suppress endogenous ovarian activity**
 - 2 tablets daily for ccHRT
- **If < 50 years old and low VTE risk**
 - Switch HRT to a COC (off-label use)
 - Change to an oral preparation (if BMI < 30 and low risk of VTE)
- **Offer 52 mg LNG-IUD**



BMI, body mass index; COC, combined oral contraceptive; HRT, hormone replacement therapy; LNG-IUD, levonogestrel intrauterine device; POP, progestogen only pill; VTE, venous thromboembolism;

Reference: 1. BMS. 2024, Management of Unscheduled Bleeding on HRT, available at: <https://thebms.org.uk/wp-content/uploads/2024/12/01-BMS-GUIDELINE-Management-of-unscheduled-bleeding-HRT-NOVEMBER2024-A.pdf> [accessed: Nov 2025]

Managing unscheduled bleeding with sequential HRT (sHRT)

- **Increase micronized progesterone dose to 300mg for 14 days every 28 days**
 - Or change to synthetic progestogen
- **Try 3-months of additional progestogen on top of current regimen**
 - Evorel sequi plus 100mg micronized progestogen or 1 norethisterone POP daily when using patch containing oestradiol and norethisterone
- **Reduce estrogen dose**
- **Offer non-hormonal alternatives**



HRT, hormone replacement therapy

Reference: 1. BMS. 2024, Management of Unscheduled Bleeding on HRT, available at: <https://thebms.org.uk/wp-content/uploads/2024/12/01-BMS-GUIDELINE-Management-of-unscheduled-bleeding-HRT-NOVEMBER2024-A.pdf> [accessed: Nov 2025]

Managing unscheduled bleeding with continuous combined HRT (ccHRT)

- **Change to an oral preparation**
 - if BMI < 30 and low risk of VTE
- **Offer 52 mg LNG-IUD**
- **Increase micronised progesterone dose to 200mg daily**
 - or change to a synthetic progestogen



BMI, body mass index; HRT, hormone replacement therapy; LNG-IUD, levonogestrel intrauterine device; VTE, veno

Reference: 1. BMS. 2024, Management of Unscheduled Bleeding on HRT, available at: <https://thebms.org.uk/wp-content/uploads/2024/12/01-BMS-GUIDELINE-Management-of-unscheduled-bleeding-HRT-NOVEMBER2024-A.pdf> [accessed: Nov 2025]; 2. <https://thebms.org.uk/publications/consensus-statements/bms-whcs-2020-recommendations-on-hormone-replacement-therapy-in-menopausal-women/> Accessed Nov 2025

Managing unscheduled bleeding with continuous combined HRT (ccHRT)

- **Try 3-months of additional progestogen on top of current preparation**
 - Evorel conti plus 100mg micronized progestogen daily or 1 norethisterone POP daily
 - If 52 mg LNG IUD in place for > 4 years, change device
- **Consider 6-month trial of sequential HRT**
 - if recently postmenopausal
- **Reduce estrogen dose**
- **Offer non-hormonal alternatives**



HRT, hormone replacement therapy; LNG-IUD, levonogestrel intrauterine device

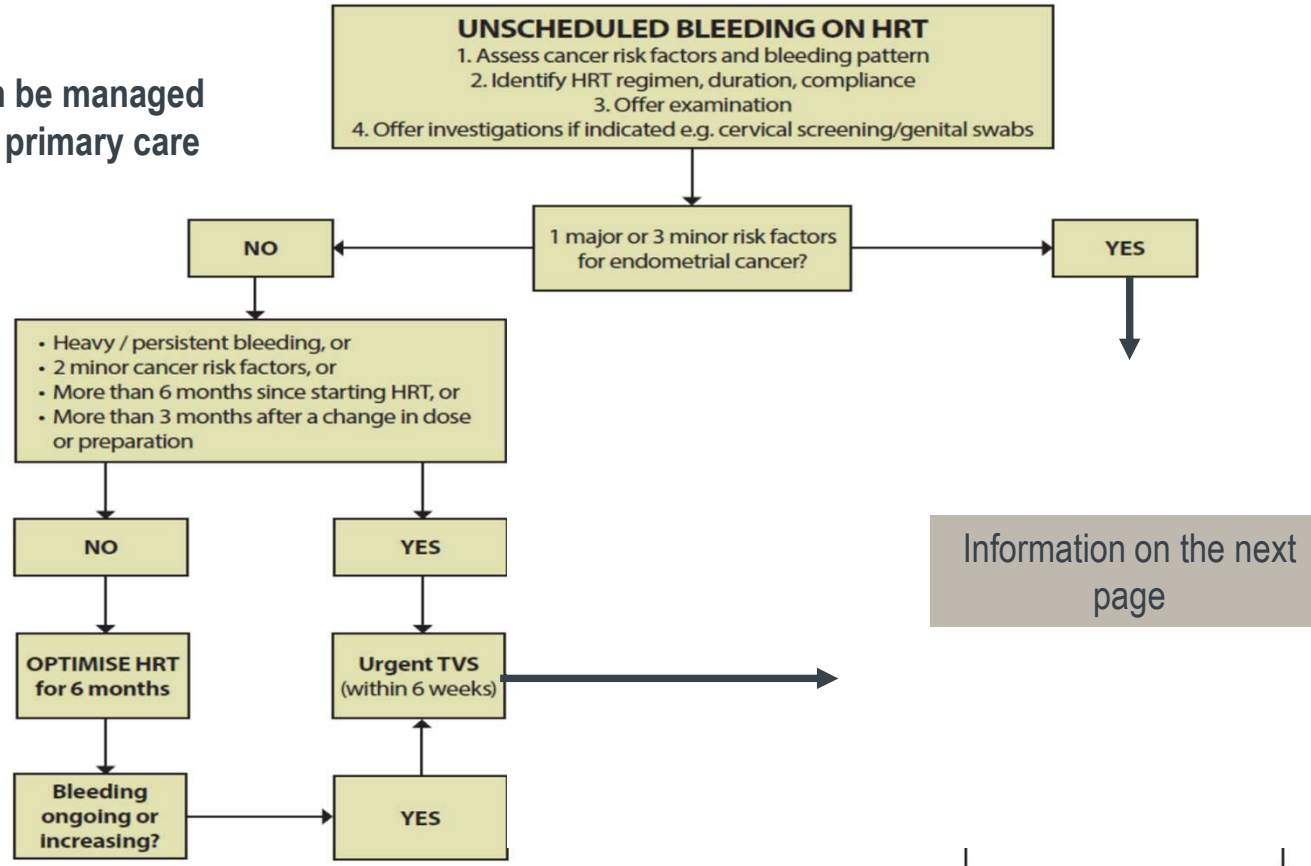
Reference: 1. BMS. 2024, Management of Unscheduled Bleeding on HRT, available at: <https://thebms.org.uk/wp-content/uploads/2024/12/01-BMS-GUIDELINE-Management-of-unscheduled-bleeding-HRT-NOVEMBER2024-A.pdf> [accessed: Nov 2025]

In the presence of a normal endometrial biopsy

- In the presence of a normal TVS and 'blind' biopsy
 - Discuss adjustments in progestogen
 - Provide **reassurance for 3 months**
- If hysteroscopy and biopsy are normal
 - Discuss adjustments in progestogen
 - Reassurance can be provided **for 6 months**

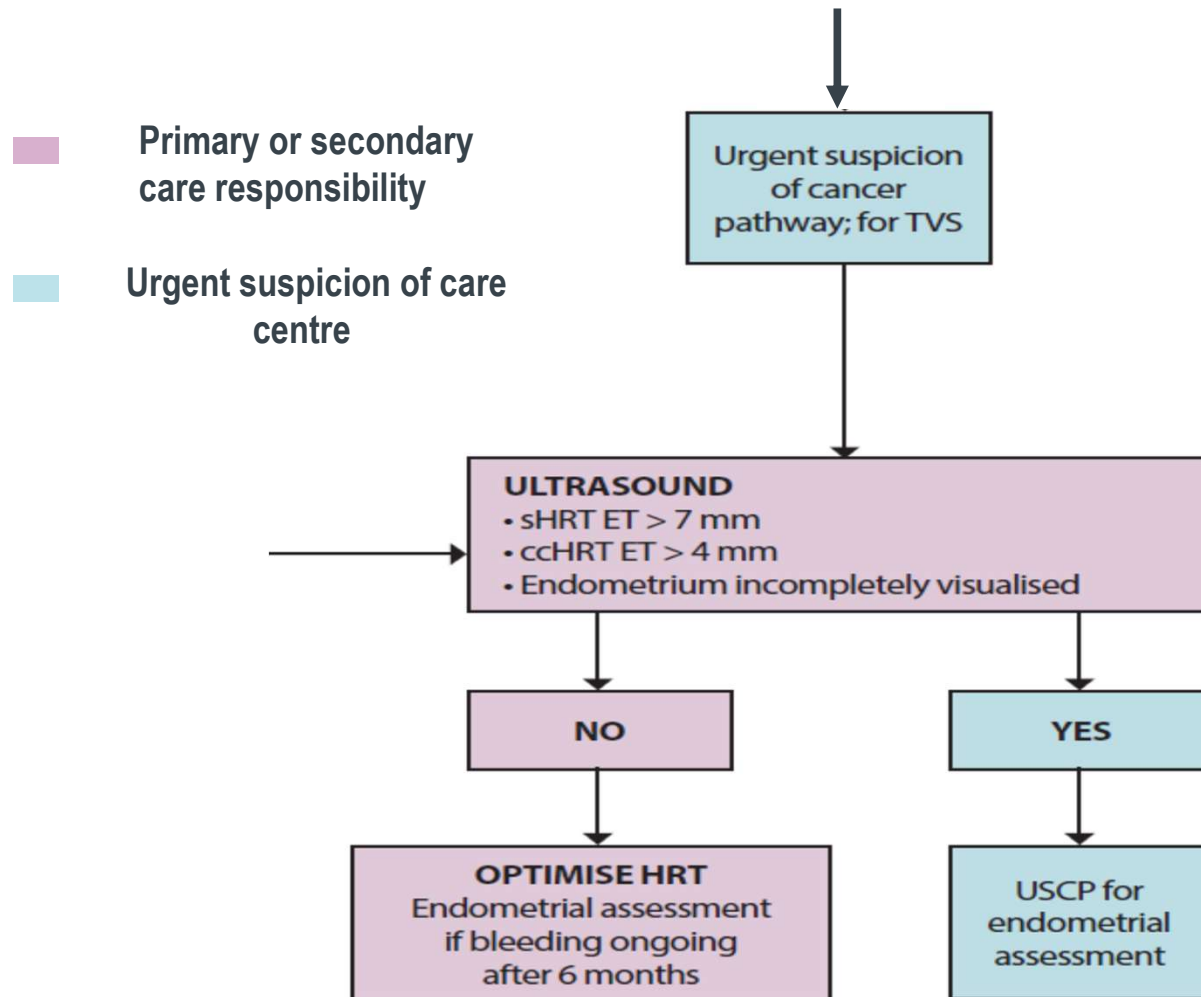


■ Can be managed by primary care



HRT, hormone replacement therapy; TVS, transvaginal ultrasound

Reference: 1. BMS. 2024, Management of Unscheduled Bleeding on HRT, available at: <https://thebms.org.uk/wp-content/uploads/2024/12/01-BMS-GUIDELINE-Management-of-unscheduled-bleeding-HRT-NOVEMBER2024-A.pdf> [accessed: Nov 2025]



ccHRT, continuous combined HRT; ET, endometrial thickness; HRT, hormone replacement therapy; sHRT, sequential HRT; TVS, transvaginal ultrasound; USCP, urgent suspicion of cancer pathway

Reference: 1. BMS. 2024, Management of Unscheduled Bleeding on HRT, available at: <https://thebms.org.uk/wp-content/uploads/2024/12/01-BMS-GUIDELINE-Management-of-unscheduled-bleeding-HRT-NOVEMBER2024-A.pdf> [accessed: Nov 2025]

Take home messages

- **Women with irregular bleeding**
 - Be aware of the 'red flags'
 - Know when to investigate/refer
- **Be able to discuss different bleeding patterns associated with HRT**
 - So women know what to expect
 - Provide options for those who want to little or no bleeding
- **When in doubt, ask a friend, use A and G**

