

# MENOPAUSE AND HRT

## Treatment and guidance

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## Housekeeping – speaker disclosures

- Financial: Honoraria from Astellas, Bayer, Besins, Exeltis, Gedeon Richter, Orion, Theramex and Viatrix for research, teaching and training  
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Clinical Director, GP and Private Menopause Specialist, Oxford Menopause Ltd

The views contained in the following slides are based on medical evidence and my own clinical experience.



## Overview of today

- 0900 - 0930 Registration
- 0930 - 1050 Menopause - the basics of assessment and diagnosis – Part 1
- 1050 - 1110 Break for coffee/tea
- 1110 - 1230 Menopause – the basics of prescribing – Part 2
- 1230 - 1330 Lunch
- 1330 - 1450 Menopause masterclass – navigating complexities
- 1450 - 1510 Break
- 1510 – 1630 Menopause masterclass – case-based discussions



# Learning Objectives

- Be confident in assessing the menopause patient – key elements to evaluate to determine options
- Be able to assess and support women with suspected premature ovarian insufficiency – primary care responsibilities
- Understand when to undertake investigations and further specialist referral
- Feel confident in explaining treatment options, and their risks and benefits to patient to allow shared decision making
- Understand the important role of lifestyle optimisation in menopause care
- Be confident in prescribing hormonal and non-hormonal treatments to patients and explaining how they are administered to ensure safe, evidence-based prescribing
- Feel confident at understanding the role of medications prescribed 'off label' including testosterone and their monitoring
- Be confident in assessing and managing patients who present with unscheduled bleeding, lack of response to treatment and those with complex co-morbidities including epilepsy, migraine, thromboembolic and vascular disease and cancer



# Menopause - the basics of assessment and diagnosis

- The Menopause Consultation
- Diagnosing menopause
- Investigations – what is needed?
- Premature ovarian insufficiency – special considerations
- Risks and benefits of HRT



# Menopause

- Menopause – cessation of menstrual cycle resulting from ovarian failure.
- Perimenopause – from first biochemical/physical changes to 12 months after LMP
- Postmenopause – 12/12 after LMP
- Average age at menopause in UK is 51
  - 80% menopausal by 54 years
  - 96% menopausal by 55 years
  - 1% of women natural menopause <40 years
  - 0.1% menopausal before 30 years
- < 45 = early, <40 = premature ovarian insufficiency (POI – 1-3% of women)
- Around 80% of menopausal women experience symptoms, 20% severely but only a small proportion take HRT (25-30%)



# The Menopause Landscape

- Women aged 50 and over now represent 26% of all women and girls globally
- A woman aged 60 in 2019 could expect to live to at least age 81
- Women comprise 67% of the paid global health and care workforce
- 4 million women aged 45-54 employed in the UK
- Menopause costs the economy 14 million working days/year

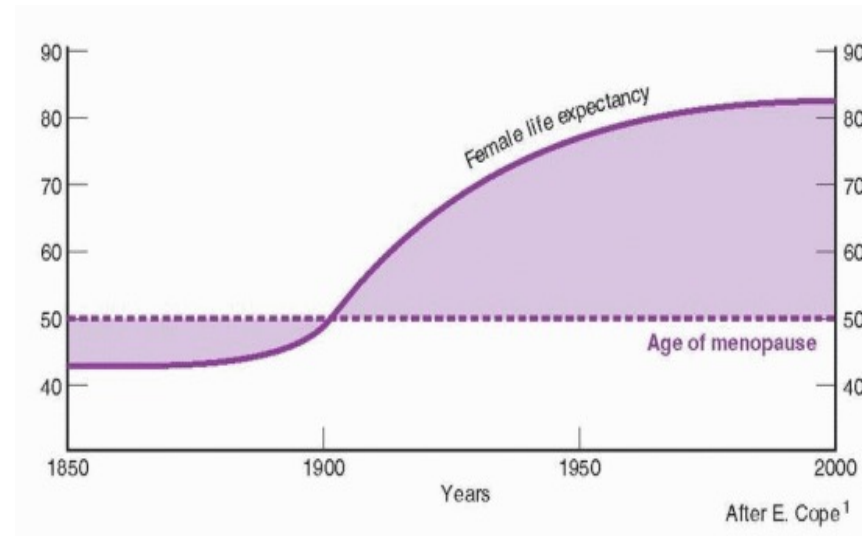


Image: <https://obgynkey.com/wp-content/uploads/2016/07/C17-TT1.gif>

	1850	2018
Life Expectancy	42	83
Age at Menopause	48	51

Chartered Institute of Personnel and Development (CIPD)  
WHO 2021



## Menopause – symptoms

- Menopause is a unique experience, around 80% women experience physical and/or psychological symptoms at some stage, 20% have severe symptoms
- Menstrual disturbance (cycle shorter, longer gaps, change in menstrual flow)
- Vasomotor - hot flushes, sweats
- Sleep issues – insomnia (tiredness, irritability, poor concentration)
- Psychological symptoms - depression, anxiety
- Memory loss ‘brain fog’, loss of confidence/self-esteem, poor concentration
- Skin and hair changes (dry, itchy, joint pains, IV disc loss)
- Headaches
- Palpitations
- Vaginal symptoms - dryness, pain, discharge, bleeding
- Sexual issues – loss of libido, arousal, orgasm (often higher post BSO)



## Symptom Checker

Do you have any of these symptoms of perimenopause (if you still have periods) or menopause (periods have stopped for over a year)?

Symptoms	Y/N	Symptoms	Y/N
Heart beating quickly or strongly		Feeling dizzy or faint	
Feeling tense or nervous		Pressure or tightness in head	
Difficulty in sleeping		Parts of body feel numb	
Excitable		Headaches	
Attacks of anxiety, panic		Muscle and joint pains	
Difficulty in concentrating		Loss of feeling in hands or feet	
Feeling tired or lacking in energy		Breathing difficulties	
Loss of interest in most things		Hot flushes	
Feeling unhappy or depressed		Sweating at night	
Crying spells		Loss of interest in sex	
Irritability		Urinary or vaginal dryness symptoms	

**If you still have periods, how often are they? Are they heavy, light?**

**Use this space to note your main concerns or questions for your GP**

Symptoms	Not at all 0	A little 1	Quite a bit 2	Extremely 3	Comment
Heart beating quickly or strongly					
Feeling tense or nervous					
Difficulty in sleeping					
Memory problems					
Attacks of anxiety, panic					
Difficulty in concentrating					
Feeling tired or lacking in energy					
Loss of interest in most things					
Feeling unhappy or depressed					
Crying spells					
Irritability					
Feeling dizzy or faint					
Pressure or tightness in head					
Tinnitus (ringing or buzzing in the ear)					
Headaches					
Muscle and joint pains					
Pins and needles in any part of the body					
Breathing difficulties					



# The Menopause Consultation

- What symptoms does the woman have? What is bothering her? How long have they been an issue? Remember to ask about vulvo-vaginal symptoms and sexual dysfunction, many women do not volunteer this information.
- Current bleeding pattern – has this changed? Does this need investigating first?
- Has she tried anything already? If so, what (including over the counter medications), did they help, any side effects?
- Past medical history – VTE, migraine, cardiac issues, breast concerns, gynaecological history, contraception
- Social history – smoking status, alcohol, exercise
- Family history – breast, ovarian, endometrial cancer, osteoporosis, cardiovascular and cerebrovascular disease, dementia
- Examination – BP, BMI, vaginal examination if required

# Menopause Investigations

- >45 with symptoms no need for bloods
- COCP/POP/depo/implant- bloods unhelpful
- Consider FSH if age 40-45 with symptoms
- Consider FSH if age <40 (1 reading >25 diagnostic of POI with >4/12 oligomenorrhoea) **ESHRE update 2024**
- FSH does not predict fertility status or final ovarian failure
- AMH/estradiol/progesterone unhelpful





# Fracture risk assessment - FRAX



## Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **UK** Name/ID:  [About the risk factors](#)

**Questionnaire:**

1. Age (between 40 and 90 years) or Date of Birth  
 Age:  Y:  M:  D:

2. Sex  Male  Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture  No  Yes

6. Parent Fractured Hip  No  Yes

7. Current Smoking  No  Yes

8. Glucocorticoids  No  Yes

9. Rheumatoid arthritis  No  Yes

10. Secondary osteoporosis  No  Yes

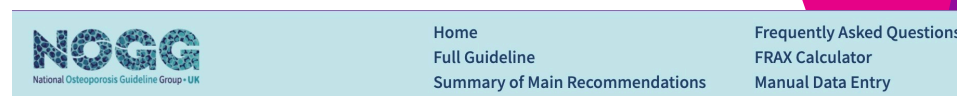
11. Alcohol 3 or more units/day  No  Yes

12. Femoral neck BMD (g/cm<sup>2</sup>)  
 Select BMD

**BMI: 22.9**  
 The ten year probability of fracture (%)

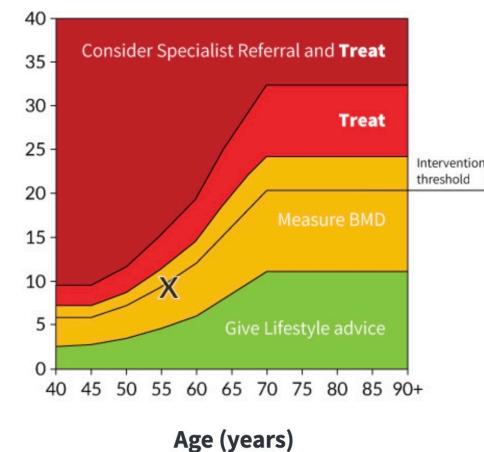
without BMD	
Major osteoporotic	<b>9.4</b>
Hip Fracture	<b>0.8</b>

[View NOGG Guidance](#)



## Intervention Thresholds

(%) 10-year probability of Major Osteoporotic Fracture



## Premature Ovarian Insufficiency (POI)

- Loss of ovarian activity occurring in women under 40 years of age
- Treatments of choice are HRT (or COCP)– until at least the average age of natural menopause NICE 2015.
- Untreated POI increases the risk of osteoporosis, CVD, Alzheimer’s disease, cognitive decline and neurological diseases.
- Diagnosis has life-changing physical and emotional consequences
- May be associated with intermittent resumption of activity in over 25% of women
- Estimates suggest it occurs in 1% of the population (higher in Sweden 1.9%)

## Premature Ovarian Insufficiency (POI)

- Etiology unknown in 70-90% of women
- Genetic factors -30% of women with POI have a FHx early menopause (Turner syndrome, fragile X (FMR1) and others)
- Autoimmune – up to 30% cases (Hashimoto's, T1DM, adrenal insufficiency, Sjogren's, rheumatoid arthritis, IBD, MS, coeliac, myasthenia gravis and alopecia)
- Rarely – mumps, HIV, TB, malaria, varicella, CMV, galactosemia
- Iatrogenic – chemotherapy, radiotherapy, surgery



## Why is POI important to recognize?

- It is well recognized that POI is associated with an increased incidence of cardiovascular and cerebrovascular disease
  - Tao et al (2016) - 48% higher risk of IHD in POI compared with menopause>50
- Osteoporosis is a key concern for women with POI, prevalence ranges from 8-27%
- Women with POI are at increased risk of cognitive impairment, stroke and Parkinson's disease
- No evidence of adverse effects of HRT on brain function before the age of natural menopause
- Management includes DEXA, risk factor identification, HRT, lifestyle intervention
- In young women the benefits of HRT far outweigh the risks
- Use of HRT in young women does not increase breast cancer risk compared to normally menstruating women

# Management of POI

## 1) Lifestyle advice

## 2) Estrogen replacement - all women should be offered estrogen replacement unless contra-indicated

- Alleviates symptoms (vasomotor, urogenital, mood, cognition, energy, musculoskeletal issues)
- Facilitates development of secondary sexual characteristics
- Improves QOL
- Minimises long-term risks of POI

### COCP vs HRT

- POISE study (HRT vs COCP in POI) –large long-term prospective multicentre study commenced in 2020
- Don't forget to consider contraception (5% chance of natural conception)
- Recommend women continue HRT until at least the average of menopause (51 in UK)



## What should we aspire to provide...

- Individualised, evidence-based advice and treatment
- Equality of access to advice and treatment
- A choice of treatment based on personal preferences, benefits and risks
- Detailed information and links to resources that are accurate
- Support in the workplace
- The ability to continue to achieve their full potential during the perimenopause and post-menopause



# Lifestyle Modification

- **Diet**

- Mediterranean-style diet
- Calcium (1000mg) and vitamin D (1000iu) daily
- Reduce sugar intake (<30g/day free sugar)
- Limit alcohol to less than 14 units/week

- **Exercise**

40% of adult women in the UK are not getting enough exercise

Benefits of exercise

- Bone mineral density
- Muscles
- Cardiovascular health
- Mood (endorphins, de-stress)
- Maintain a healthy weight

- **Smoking**

- increases menopausal symptoms
- increased CVD risk
- Increased osteoporosis risk

- **Vasomotor symptoms and sleep**

- Loose clothing, natural fabrics
- Avoid spicy food, caffeine, alcohol
- Fans, remove heavy bedclothes
- Avoid screen time
- Consistent bedtime



# Patient resources

Women's Health Concern logo and navigation menu: Home, Help and advice, News, Events, Shop, Support us, For professionals, Media hub. Search bar and 'Donate with JustGiving' button are also visible.

**For patients**  
Women's Health Concern (WHC), established in 1972 and the patient arm of the BMS since 2012. WHC provides a confidential, independent service to advise, inform and reassure women about their gynaecological, sexual and post reproductive health.

**BBC One – Panorama: The Menopause Industry**  
30 September 2024

It is possible that the issues raised in the BBC One Panorama programme may be causing you to be concerned about your menopause treatment. Taking HRT, which is prescribed in line with national guidance, generally provides more benefits than risks. The type and duration of use can be discussed at your next routine review (which should be at least annually). If you have any concerns about your menopause treatment, please contact your own GP or other health professional.

**PANORAMA**

**BMS PPMC Resources Toolkit**  
Evidence-based, peer-reviewed BMS and WHC resources, answering the key questions in menopause care.

**Contraception: The Answers You've Been Looking For**  
A guide to help you decide what contraception works best for your body. [More details >](#)

Women's Health Concern logo and navigation menu: Home, Help and advice, News, Events, Shop, Support us, For professionals, For the press. Search bar and 'Donate with JustGiving' button are also visible.

## Menopause Wellness Hub

However you choose to manage your menopause symptoms, your lifestyle choices are going to be the cornerstone of any treatment plan you choose.

Hormone Replacement Therapy (HRT), Cognitive Behavioural Therapy (CBT) and other complementary and alternative treatments can all be very helpful, but the transition to menopause is a good time to review your lifestyle. Not only can this help manage menopausal symptoms in the short term, it can lay the foundations for good health through perimenopause, menopause, and the years to come.

The resources on this page offer evidence-based, peer reviewed information to women and their partners.

- Menopause: Weight gain, nutrition and lifestyle**  
Nigel Denby, Registered Dietician, answers a number of questions.
- Menopause: Continuing the conversation – A holistic approach to menopause**

**Help and advice**

- > Find a BMS Menopause Specialist
- > Email advisory service
- > WHC factsheets and other helpful resources
- > Menopause Wellness Hub
- > BMS TV videos
- > Menopause in the Workplace

[www.womens-health-concern.org/](http://www.womens-health-concern.org/)

Language

English

Country

United Kingdom

Language

English

Country

United Kingdom

Step  
2 of 2

Are you getting

## ENOUGH CALCIUM ?

**YOUR ESTIMATED DAILY CALCIUM INTAKE IS**

**700 mg**

**YOUR RECOMMENDED DAILY CALCIUM INTAKE IS**

**1200 mg**

## WHAT DOES THIS MEAN?

**You may not be getting enough calcium.**

## HRT : Risk/benefit discussion

In the majority of women under 60, benefits of HRT outweigh risks.

- Benefits

- 1) Relief of menopause symptoms both psychological and physical, including sexual function
- 2) Reduced risk of CHD
- 3) Reduced risk of osteoporosis
- 4) Potential positive impact on dementia (?)
- 5) Improved glucose tolerance
- 6) Reduced risk of colorectal cancer

- Risks

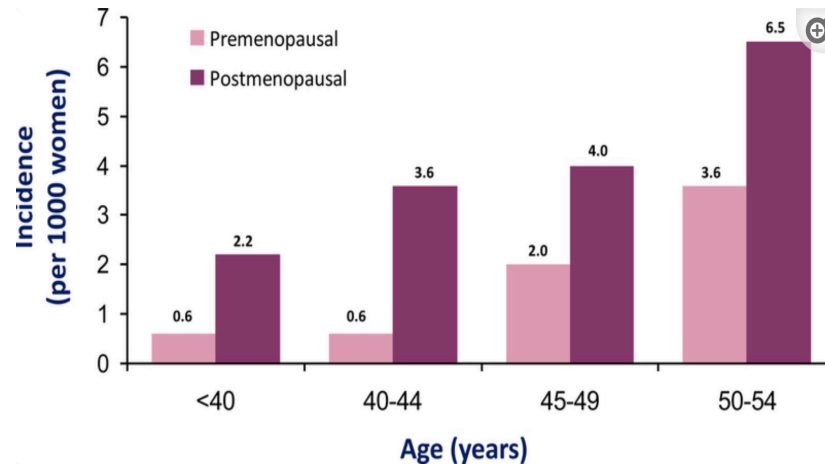
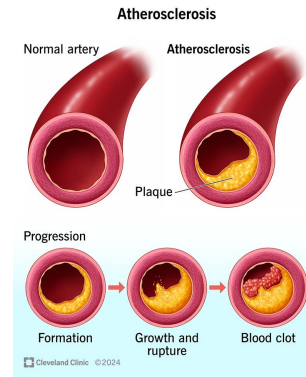
- 1) Breast cancer – age/preparation
- 2) VTE – preparation dependent
- 3) CVA – age/preparation dependent
- 4) Endometrial cancer – reduced with addition of progestogen

# Benefits of HRT

## Cardiovascular Disease

Evidence suggests a ‘window of opportunity’ for HRT (estrogen with or without progesterone)

- started before the age of 60 or within 10 years of the menopause
- associated with a reduction in atherosclerosis progression, coronary heart disease and death from cardiovascular causes as well as all-cause mortality



Salpeter SR, Walsh JME, Greyber E, Salpeter EE. J Gen Intern Med 2006;21:363–366  
 Hodis HN, Mack WJ. Cancer J. 2022; 28(3):208-223



# Osteoporosis and menopause

- The National Osteoporosis Guideline Group estimates that 536,000 fractures are caused by osteoporosis in the UK.
- Mortality rates with femur fractures are estimated to be 20% within the first year.
- Advice should be given to menopausal women regarding lifestyle modification and bone health.
- HRT has been shown to have a significant protective effect against osteoporosis and related fragility fractures and preventing osteoporosis in both spine and hip.

**Evidence from RCTs showed a significant reduction in the risk of any fracture in women using HRT compared with women not using HRT.**

NICE menopause guideline review assessed 20 RCTs that included sample sizes from 36 to 16,608 cases and 21 comparative cohort studies which included sample sizes from 157 to 170,852 cases.

1. Hamoda et al. (2020) BMS Consensus Statement – HRT in menopausal women, Post Reproductive Health 2020, page 7; Vol. 26(4) 181–208.

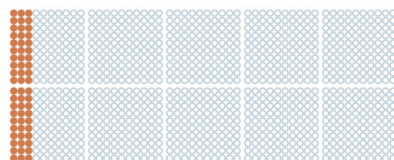
# Benefits of HRT- Osteoporosis

Women aged 45 or over

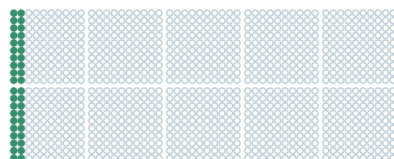
## Combined HRT: osteoporosis

In this section, fragility fractures are used as a marker of osteoporosis.

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):

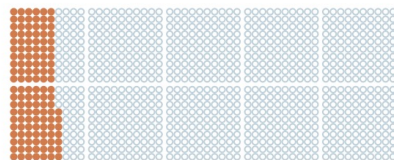


60 women out of 1,000 women who **never take HRT** experience a fragility fracture, 940 do not.

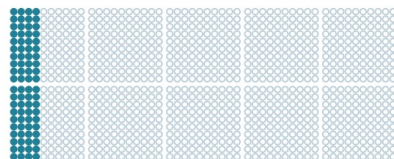


40 women out of 1,000 women who **take HRT for 5 years** from the age of 50 experience a fragility fracture, 960 do not. This is 20 fewer women, compared to women who never take HRT.

On average, between the ages of 50 and 59 (that is, when measuring over 10 years):



127 women out of 1,000 women who **never take HRT** experience a fragility fracture, 873 do not.



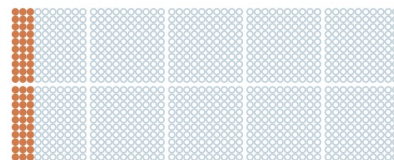
80 women out of 1,000 women who **take HRT for 10 years** from the age of 50 experience a fragility fracture, 920 do not. This is 47 fewer women, compared to women who never take HRT.

Women aged 45 or over

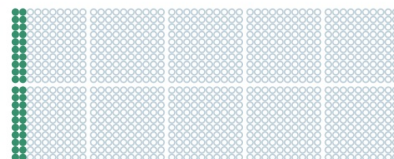
## Oestrogen-only HRT: osteoporosis

In this section, fragility fractures are used as a marker of osteoporosis.

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):

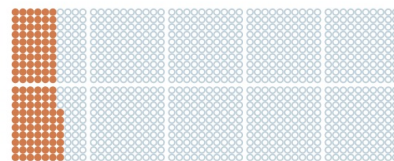


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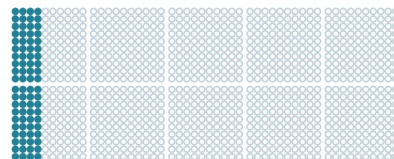


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## Venous thromboembolism (VTE) and Stroke

- Baseline VTE risk - 1.7 per 1000 women per year in women over 50
- The risk of stroke is age related - overall the risk is low in women <60

### Oral estradiol

- VTE - additional 1.5 events per 1000 women per year
- CVA - associated with a small increase in the risk of stroke (dose related)

### Transdermal estradiol

- VTE - no significant increased risk (OR 0.93)
- CVA - unlikely to increase the risk of stroke above baseline risk

### Vaginal estrogen

- no significant increase in risk

Consider micronised progesterone/dydrogesterone with transdermal estradiol in women who are at increased risk

## Breast cancer

- Most commonly occurring female cancer in developed countries
- 11,500 women die from breast cancer in UK every year, prognosis improving +
- Lifetime risk 1 in 7
- Gene mutations in breast cells initiates breast cancer but progression and development depends on other lifestyle and reproductive factors
- Most women (90%) diagnosed with breast cancer are considered to be at population risk with the gene mutations developing during their lifetime
- 10% of women are at an elevated risk due to a family history with an inherited gene mutation

## Risk factors for breast cancer

- Gender – F:M 200:1
- Increasing age (majority (80%) diagnosed >50)
- Family history
- ‘High risk’ benign breast conditions
- Lifestyle and reproductive factors
  - prolonged exposure to endogenous estrogen
  - exogenous hormone exposure
  - obesity
  - alcohol
  - lack of physical activity



# Breast Cancer risks

Breast Cancer	Absolute excess risk per 1000 women aged 50-59 over 5 yrs
Overweight (BMI 25-29.9)	+4
Obese (BMI >30)	+10
Current smoker	+3
4-6U alcohol/day	+8
>6U alcohol/day	+11
>2.5hrs exercise/week	-7

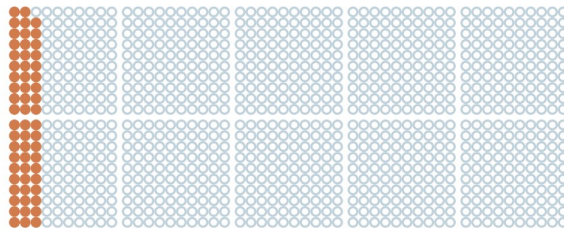
Breast Cancer	No of cases	Absolute excess risk per 1000 women aged 50-69 (over 20 yrs)
No HRT	59	
Combined HRT 5 yrs use	79	20
Combined HRT 10 yrs use	92	33
Oestrogen only HRT 5yrs	69	10
Oestrogen only HRT 10 yrs	71	12

BMS Consensus Statement – The benefits and risks of HRT before and after a breast cancer diagnosis  
 NICE – Menopause NG 23, updated 2024.

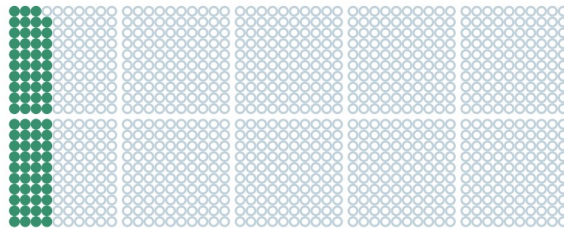
Women aged 45 or over

## Combined HRT: breast cancer

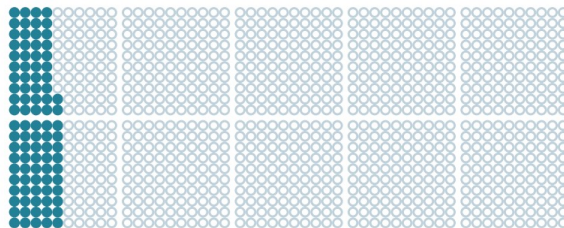
On average, between the ages of 50 and 69 (that is, when measuring over 20 years):



59 women out of 1,000 women who **never take HRT** develop breast cancer, 941 do not.



79 women out of 1,000 women who **take combined HRT for 5 years** from the age of 50 develop breast cancer, 921 do not. This is 20 more women, compared to women who do not take HRT.



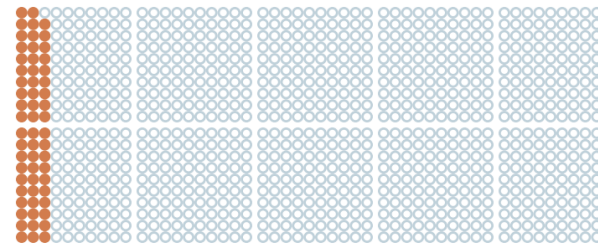
92 women out of 1,000 women who **take combined HRT for 10 years** from the age of 50 develop breast cancer, 908 do not. This is 33 more women, compared to women who do not take HRT.

Note: These graphs cover continuous and sequential combined HRT together.

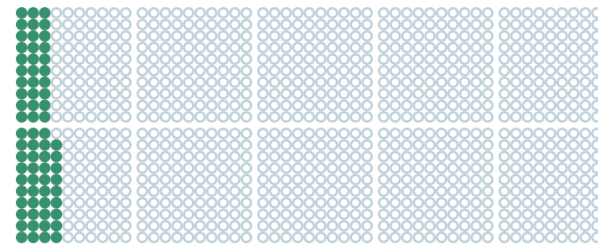
Women aged 45 or over

## Oestrogen-only HRT: breast cancer

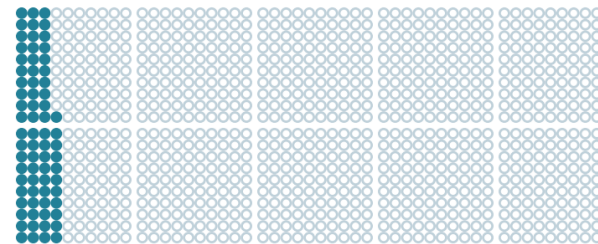
On average, between the ages of 50 and 69 (that is, when measured over 20 years):



59 women out of 1,000 women who **never take HRT** develop breast cancer, 941 do not.



69 women out of 1,000 women who **take oestrogen-only HRT for 5 years** from the age of 50 develop breast cancer, 931 do not. This is 10 more women, compared to women who do not take HRT.



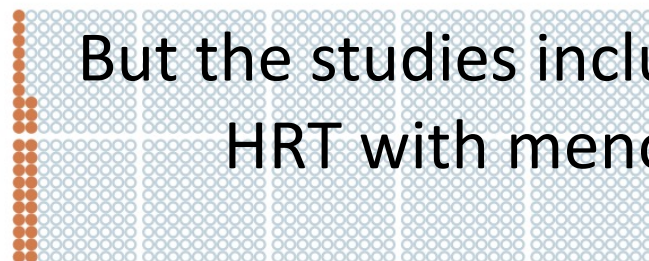
71 women out of 1,000 women who **take oestrogen-only HRT for 10 years** from the age of 50 develop breast cancer, 931 do not. This is 12 more women, compared to women who do not take HRT.

# What about younger women?

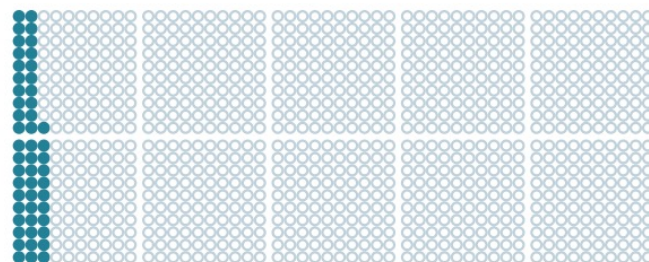
Early menopause (women aged 40 to 44)

## Combined HRT: breast cancer

On average, between the ages of 40 and 59 (that is, when measuring over 20 years):



33 women out of 1,000 women who take HRT develop breast cancer, 967 do not.

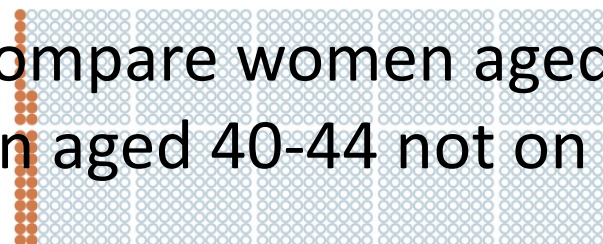


51 women out of 1,000 women experiencing early menopause who take combined HRT for 10 years from the age of 40 develop breast cancer, 949 do not. This is 18 more women, compared to women who do not take HRT.

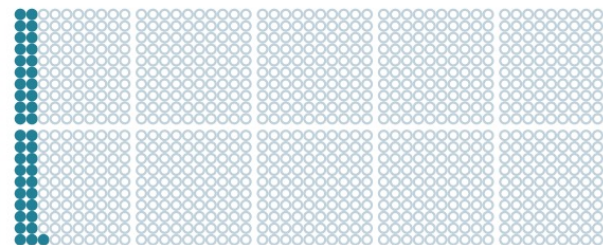
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## Oestrogen-only HRT: breast cancer

On average, between the ages of 40 and 59 (that is, when measuring over 20 years):



33 women out of 1,000 women who never take HRT develop breast cancer, 967 do not.



41 women out of 1,000 women experiencing early menopause who take oestrogen-only HRT for 10 years from the age of 40 develop breast cancer, 959 do not. This is 8 more women, compared to women who do not take HRT.

But the studies included did not compare women aged 40-44 on HRT with menopausal women aged 40-44 not on HRT!

## Progestogens and breast cancer risk

- Estrogen plus micronized progesterone – no significant increase in breast cancer risk for up to 5 years use (HR 1.11)
- Estrogen plus micronized progesterone >5 years associated with a small increase in breast cancer risk (HR 1.31)
- No difference in risk with oral vs transdermal estradiol
- LNG-IUS plus estrogen – similar risk to regimens containing oral progestogens

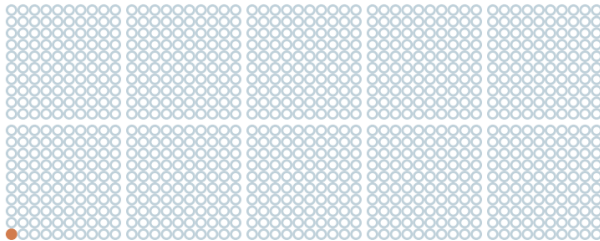
E3N cohort study, Fournier et al (2014) ; Finnish Cancer Registry

# Risks of HRT – Ovarian cancer

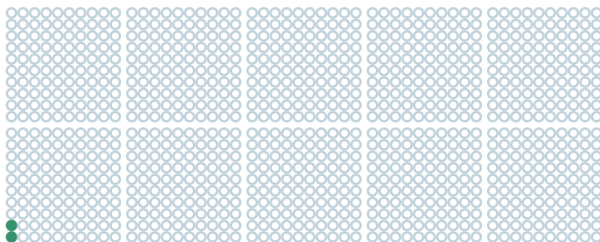
Women aged 45 or over

## Oestrogen-only HRT: ovarian cancer

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



1 woman out of 1,000 women who **never take HRT** develops ovarian cancer, 999 do not.

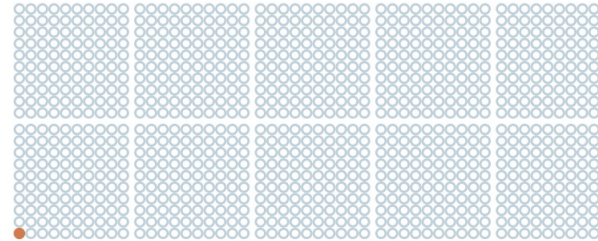


2 women out of 1,000 women who take **oestrogen-only HRT** from the age of 50 for an **unknown duration** develop ovarian cancer, 998 do not. This is 1 more woman, compared to women who never take HRT.

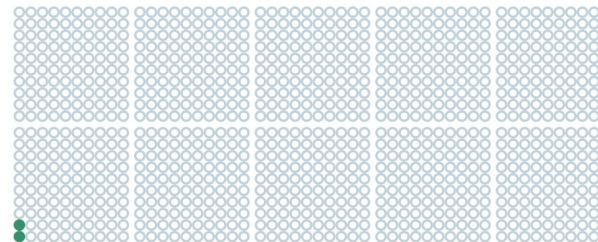
Women aged 45 or over

## Combined HRT: ovarian cancer

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



1 woman out of 1,000 women who **never take HRT** develops ovarian cancer, 999 do not.



2 women out of 1,000 women who take **combined or oestrogen-only HRT** for an **unknown duration** from the age of 50 develop ovarian cancer, 998 do not. This is 1 more woman, compared to women who never take HRT.

# Risks of HRT – endometrial cancer

## Endometrial cancer

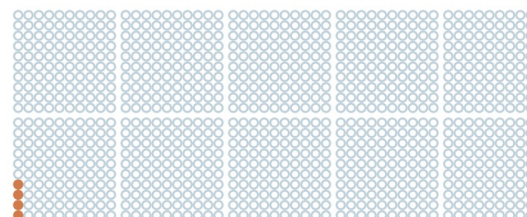
- Unopposed estrogen therapy increases the incidence of endometrial cancer, this risk is ameliorated by the use of progestogens alongside estrogen in women with an intact uterus
- The WHI study reported a neutral effect on the risk of endometrial cancer with HRT cf. placebo (5yrs HRT use)

NICE NG23

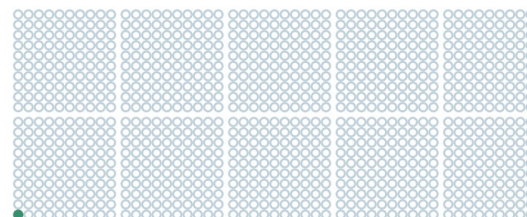
Women aged 45 or over

## Combined HRT: endometrial cancer

On average, between the ages of 50 and 54 (that is, when measuring over 5 years):



4 women out of 1,000 women who never take HRT develop endometrial cancer, 996 do not.



1 woman out of 1,000 women who take continuous combined HRT for an unknown duration from the age of 50 develop endometrial cancer, 999 do not. This is 3 fewer women, compared to women who never take HRT.



8 women out of 1,000 women who take sequential combined HRT from the age of 50 for an unknown duration develop endometrial cancer, 992 do not. This is 4 more women, compared to women who never take HRT.

# Dementia and HRT

- BMS/WHC – 2020

‘ based on current evidence, women should be reassured that HRT is unlikely to increase the risk of dementia or to have a detrimental effect on cognitive function in women initiating HRT before the age of 60’

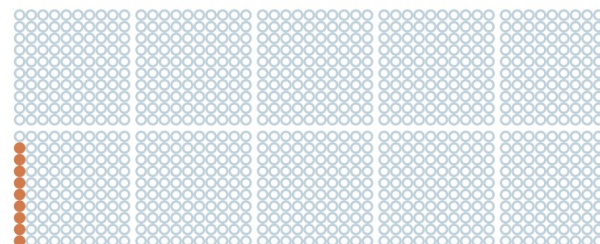
- HRT should **NOT** be initiated for the sole purpose of improving cognitive function or reducing the risk of dementia in postmenopausal women

- RCTs have shown impaired verbal recall in women with vasomotor symptoms (<https://pubmed.ncbi.nlm.nih.gov/18562950/>)

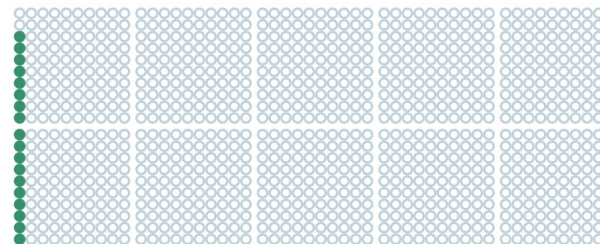
Women aged 45 or over

## Combined HRT started after 65: dementia

On average, over a 4-year period starting when they are age 65 or over:



9 women out of 1,000 women who never take HRT develop dementia, 991 do not.



18 women out of 1,000 women who take combined HRT for 4 years, starting at age 65 or over, develop dementia over the same 4-year period, 982 do not. This is 9 more women, compared to women who never take HRT.



Quick break....



# Menopause – the basics of prescribing

- Practical prescribing including progestogens
- Genitourinary syndrome of menopause
- Non-hormonal treatment options
- Managing unscheduled bleeding on HRT
- Case studies



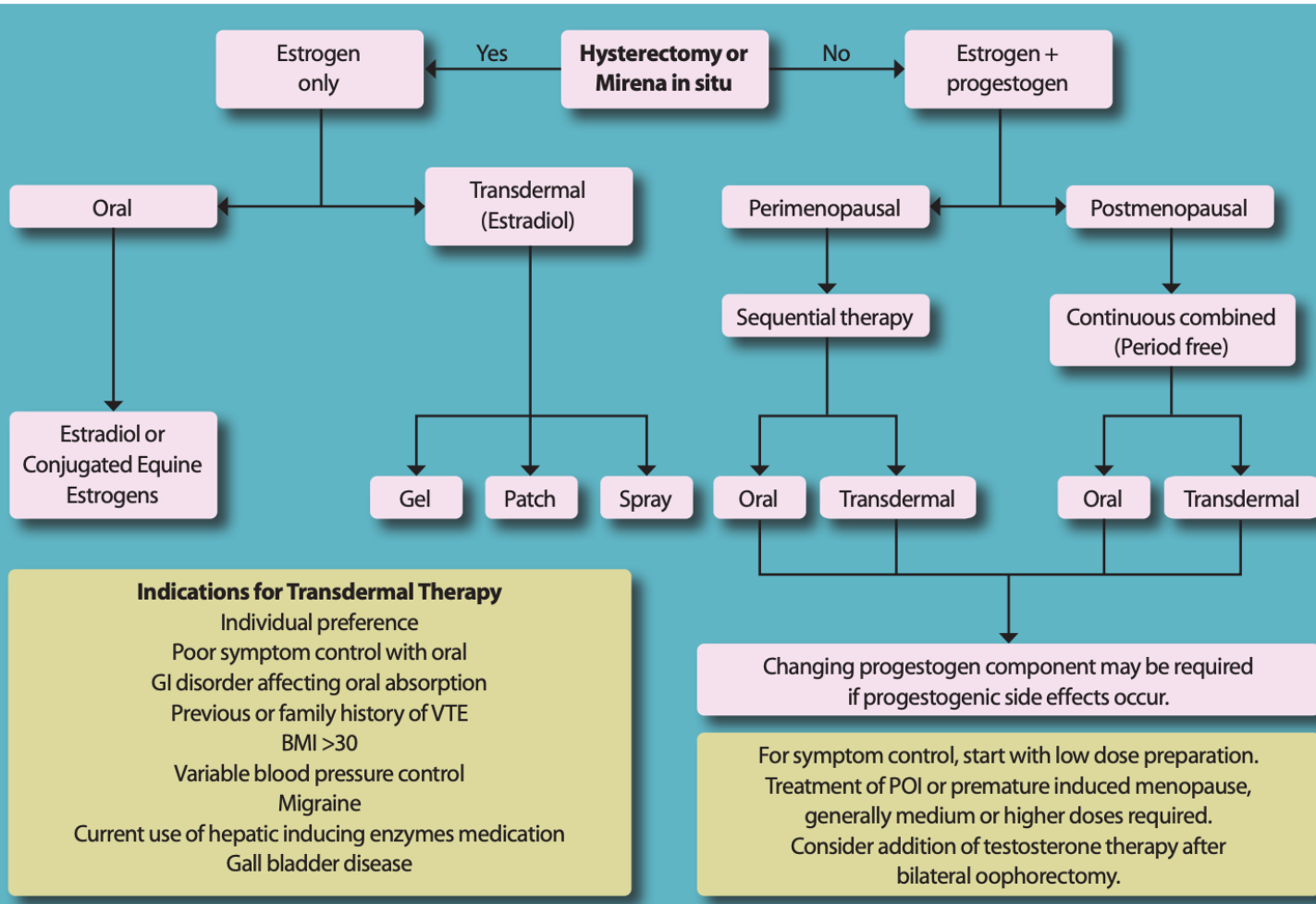
# Menopause Treatment Options

- Individualised care is key
- Address lifestyle factors – weight, smoking, alcohol, exercise, caffeine
- Opportunity to ensure cervical screening, mammography up to date, look at ongoing long term health risks
- Hormonal vs non-hormonal options
- Vaginal treatments

# HRT – what to prescribe?

- Combined HRT (estrogen and progestogen) – women with a uterus
  - sequential – perimenopausal women (<12/12 amenorrhoea)
  - continuous combined – postmenopausal
  - 52mg LNG-IUD can be used in both peri and post-menopausal women as the progestogen component of HRT
- Unopposed estrogen
  - hysterectomized women  
(caution – endometriosis/subtotal hysterectomy)
- Tibolone
  - postmenopausal women
- Topical estrogen therapies
  - prescribed in isolation or combined with HRT

- <https://www.nice.org.uk/guidance/ng23/chapter/Recommendations#long-term-benefits-and-risks-of-hormone-replacement-therapy>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8417494/>



# Choice of HRT

## Advantages/disadvantages

Oral combined preparations	Gel (daily)	Patches (twice weekly)	Spray (daily)
<p><b>Appropriate</b> dose of estrogen/progestogen</p> <p><b>Minimises</b> patient errors</p> <p><b>Easy</b> to use</p>	<p><b>Lower</b> VTE risk vs oral</p> <p><b>Easy</b> to adjust/invisible</p> <p><b>Patient compliance essential</b> – takes time to dry</p> <p><b>Requires progestogen</b> in sequential or continuous regimen</p>	<p><b>Lower</b> VTE risk vs oral</p> <p><b>Visible</b> on skin, can leave residue</p> <p><b>Skin irritation</b> can occur</p> <p>Dose adjustments with combined patches <b>more difficult</b></p> <p><b>Requires progestogen</b> in sequential or continuous regimen</p>	<p><b>Lower</b> VTE risk vs oral</p> <p><b>Quick</b> drying</p> <p>Dose adjustments more <b>difficult</b></p> <p><b>Requires progestogen</b> in sequential or continuous regimen in addition</p>

## Estradiol – equivalent doses

**Table 2: 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



# Transdermal estrogen – application

Provide clear instructions to patients – improves compliance/efficacy

Offer choice, skin should be clean/dry (no moisturiser/sun cream!)

## Patches

- below the waist, ideally buttock/thighs
- massage the patch for 30 secs (improves adherence)
- adhesive residue easily removed with baby oil/surgical spirit

## Spray

- prime a new pack before use (3 sprays with the cover on)
- apply cone to inner forearm and spray
- if using >1 spray do not overlap spray sites
- allow to dry for 2 minutes before dressing
- avoid washing/bathing for 1-2 hours

## Gel

- use the lid as an applicator (pump)
- smear the gel in a thin layer on the inner thigh or upper outer arm
- 1 pump one location
- allow to dry before dressing
- avoid bathing for 2 hours
- wash hands

# Roles and effects of progestogens in HRT

Unopposed estrogen	Non-hysterectomized women	Up to 5 years use	>5yrs use of sequential combined HRT
<p>Associated with <b>significant increased risk</b> of endometrial hyperplasia</p> <p><b>Dose and duration dependent</b> with exposure between 1-3 years</p>	<p>Required <b>daily</b> in a continuous combined regimen</p> <p>Require progestogen administered for <b>12-14 days</b> in a sequential regimen</p> <p>Women <b>taking sequential HRT with &lt;10 days</b> of progestogen are at increased risk of endometrial hyperplasia and cancer</p>	<p>Progestogen intake in <b>recommended doses for 12–14 days a month</b></p> <p><b>Does not appear to be associated</b> with a significant increase in risk of endometrial hyperplasia</p> <p>Progestogen compliance required</p>	<p>Associated with a <b>small increase in risk of endometrial hyperplasia and endometrial cancer</b></p> <p>Risk is <b>dose and duration dependent</b> in relation to progestogen intake</p>

## Progestogens - doses

**Table 3: Progestogen dose per licensed estrogen dose in the baseline population**

Estrogen dose	Micronised Progesterone		Medroxy progesterone		Norethisterone		LNG-IUD (52mg)
	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
Standard	100 mg	200 mg	2.5-5 mg	10 mg	5 mg*	5 mg*	
Moderate	100 mg	200 mg	5 mg	10 mg	5 mg	5 mg	
High	200 mg	300 mg	10 mg <sup>^</sup>	20 mg <sup>^</sup>	5 mg	5 mg	

\* 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).

<sup>^</sup> 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.



# Genitourinary syndrome of menopause -GSM

Offer vaginal estrogen to women with urogenital atrophy (including those on systemic HRT) and continue treatment for as long as needed to relieve symptoms.

- Think about topical estrogen in women with a variety of symptoms suggestive of GSM – skin issues (itching, soreness, inflammation), prolapse, bladder issues, sexual difficulties
- For the majority of women in whom systemic HRT is contraindicated, topical estrogen can be considered
- If vaginal estrogen does not relieve symptoms of urogenital atrophy, consider increasing the dose/changing preparation. Examination vital to recognize other issues and treat appropriately.
- Explain that:
  - symptoms often come back when treatment is stopped
  - adverse effects from vaginal estrogen are very rare
  - they should report unscheduled vaginal bleeding to their GP

Don't forget to include advice about lubricants/moisturisers.



# Topical (local) estrogen options



## Estradiol (E2)

- **10mcg intravaginal tablet (POM)**

One tablet nightly 2/52 then twice weekly

One applicator for 24 tabs (wash after use)

- **10mcg intravaginal tablet (OTC)**

One tablet nightly 2/52 then twice weekly

Available over the counter (post menopause)

- **Vaginal ring(7.5mcg/24 hrs)**

Self-administered, 3/12 duration.

Can remain in during sex. Can use with ring pessary.

Licensed for 2 years, but unlicensed long-term use.

## Estriol (E3) - weaker

- **0.1% (1mg/1g) cream**

**One applicator = 0.5mg estriol**

Daily 2/52 then twice weekly

- **Pessary 30mcg (0.03mg)**

Daily 3/52 then twice weekly

- **Gel 50mcg/g**

Daily 3/52 then twice weekly

- **0.01% Cream (5ml applicator=0.5mg)**

Daily 2/52 then twice weekly

Expensive, dilute, large volume

## Newer products

### Blissel 0.005% gel

50mcg/g

Daily 3/52 then twice weekly

### Imvaggis

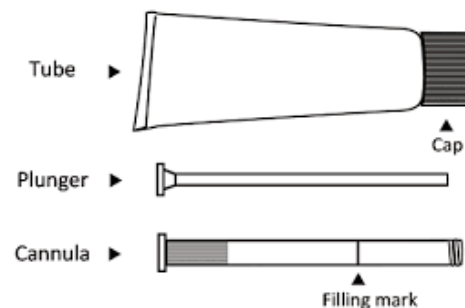
Pessary 30mcg (0.03mg)

Daily 3/52 then twice weekly

### Prasterone/Intrarosa

6.5mg vaginal pessary daily

Converted to oestrogens and androgens vaginally, useful if vaginal oestrogen ineffective/allergy





# Topical estrogen – formulary options

## BSW Formulary

**Urogenital Atrophy [listed in ascending cost order<sup>3</sup> – patient preference may influence choice of formulation]**

**Ovestin cream** 1 applicator = 500 mcg estriol

**Vagirux vaginal tabs** 1 tab = 10mcg estradiol

**Imvaggis pessary** 1 pessary = 30 mcg estriol

**Estring** 7.5mcg /24hrs (vaginal ring worn for 3 months)

**Blissel gel** 1 applicator = 50mcg estriol

## BOB ICB Formulary

### Topical Vaginal Estrogen

HRT product	Estrogen	Delivery	Strength	Indications for use
Estradiol	Estradiol	Intravaginal Pessary	10mcg	First line topical treatment option Please prescribe generically as this is more cost-effective than branded Vagirux / Vagifem
Estriol 1mg/g	Estriol	Intravaginal cream	0.1% 1mg/g (0.5mg estriol per	Most cost-effective topical HRT
Estriol 0.01%	Estriol	Intravaginal cream	0.01% 0.1mg/g (0.5mg estriol per app)	Patient or clinician preference
Blissel®	Estriol	Intravaginal gel	0.005% 50mcg/g (50mcg estriol per app)	Reduced potency estriol, for patients with side effects/ sensitivity to other topical preparations
Imvaggis®	Estriol	Intravaginal pessary	0.03mg	Less potent estriol where other preparations not tolerated/ side effects or difficulty in using other preparations
Estring®	Estradiol	Intravaginal ring	7.5mcg/24hrs over 90 days	Allergies to other topical products, dexterity problems with applicators, patient preference
Intrarosa®	Prasterone (DHEA)  (Prasterone is metabolised to estrogens and androgens, hence not to be prescribed for patients unsuitable for topical estrogens)	Vaginal pessary	6.5mg	To be prescribed only after <b>RECOMMENDATION</b> by a <b>SPECIALIST</b> . Prescribing should be <b>RESTRICTED</b> to patients who have already tried several other topical vaginal estriol / estradiol preparations but found them to be unsuitable due to lack of efficacy or intolerance / side effects.

# How to advise patients about topical estrogen

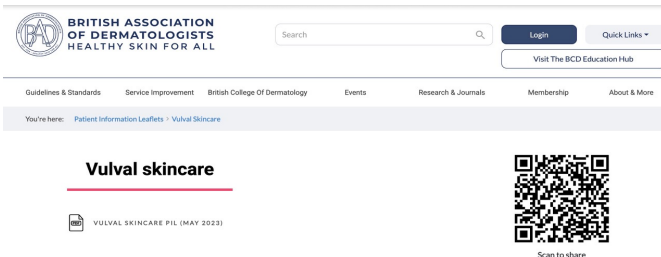
- Be patient, it can take 2-3 months for treatment to be effective
- If symptoms worsen/do not improve important to review
  - check compliance
  - what else are they applying?
  - re-examine
- Keep going, the symptoms recur if you stop
- No time limit to use but important to review annually
- If new concerns – ulcers, lumps, bleeding report to HCP
- Can be used alongside systemic HRT (including long-term)
- Side effects most common in the first 2-4 weeks
- Vulval skin care/emollients/lubricants can be used alongside (and important)



How to use Hydromol Ointment by Dr Richard Turner

Hydromol 244 subscribers [Subscribe](#) [Like](#) 231 [Share](#) [Download](#) [More](#)

[https://www.youtube.com/watch?v=2I\\_-rDuA684&t=4s](https://www.youtube.com/watch?v=2I_-rDuA684&t=4s)



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### Vulval skincare

[VULVAL SKINCARE PIL \(MAY 2023\)](#)



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## Non-hormonal treatment options

- Lifestyle changes
- Non-hormonal therapies

Some have significant impact on frequency and severity of VMS

Clonidine - 50-100mcg bd

Venlafaxine - 37.5-75mg daily

Oxybutynin - 2.5-5mg od-bd

Gabapentin - 300-1800mg daily

SSRIs - Paroxetine 10mg od, Citalopram 10/20mg, Fluoxetine 10/20mg (c/i with Tamoxifen)

CBT – mood, sleep, physical symptoms

Neurokinin 3 receptor antagonists – Fezolinetant, Elinzanetant

### Genito-urinary syndrome of menopause

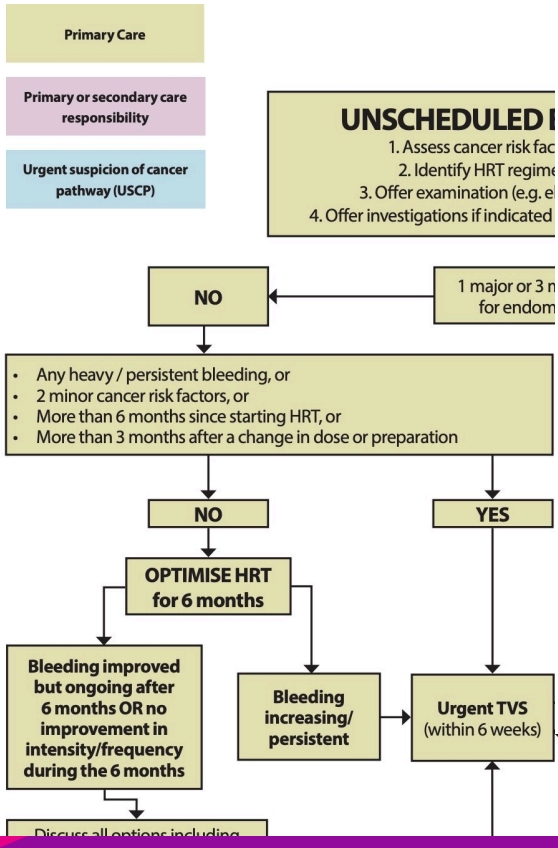
- Vaginal moisturisers are first-line (Sylk, Pjur, Hyalofemme, YES (VM/OB/WB))
- Consider low-dose topical estrogen (negligible systemic absorption, evidence from observational studies limited)
- ? Topical estrogen in women using an AI

## Assessing the woman with unscheduled bleeding

- Review bleeding pattern
- HRT regimen, compliance (missed doses, GI upset, drug interactions)
- Assess risk factors for endometrial cancer and BMI
- EXAMINE
  - abdominal/pelvic
  - cervical screening if indicated
  - swabs to exclude infection



# BMS Management



## MAJOR risk factors for endometrial cancer

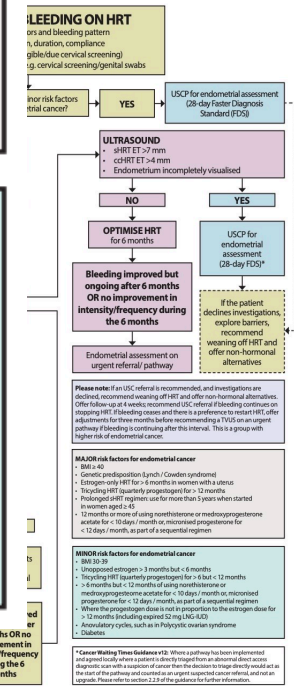
- BMI  $\geq 40$
- Genetic predisposition (Lynch / Cowden syndrome)
- Estrogen-only HRT for  $> 6$  months in women with a uterus
- Tricycling HRT (quarterly progestogen) for  $> 12$  months
- Prolonged sHRT regimen: use for more than 5 years when started in women aged  $\geq 45$
- 12 months or more 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

# HRT (2024)

## Management of unscheduled bleeding on hormone replacement therapy (HRT)



# HRT optimization – NHSE GIRFT

## Recommendations for Reducing and Managing Unscheduled Bleeding on HRT

Problem	Potential adjustment
General principles	<ul style="list-style-type: none"> <li>Assess compliance +/- order of pills or patches if using sHRT</li> <li>At initiation of HRT, consider starting with a low dose preparation</li> <li>At initiation of HRT, offer a sequential preparation if women are still menstruating and &lt; 55</li> <li>Time the start of sHRT to their natural cycle</li> <li>Offer ccHRT if a) initiating HRT and are post-menopausal or b) have been using sHRT for 5 years and are aged more than 50</li> <li>Offer the 52 mg LNG-IUD, if appropriate, to women initiating HRT, particularly if contraception is also required</li> <li>Offer change of 52 mg LNG-IUD if new onset unscheduled bleeding at 4 years of use and investigations are normal (particularly if BMI ≥ 40)</li> <li>Offer vaginal estrogen if atrophic findings on examination.</li> </ul>
Poor compliance of non-combined preparations	<ul style="list-style-type: none"> <li>Change to a combined patch</li> <li>Change to a combined oral preparation – consider one containing micronised progesterone (MP) if synthetic progestogens not acceptable</li> <li>Take MP at the same time as applying the daily gel</li> <li>Offer the 52 mg LNG-IUD.</li> </ul>
Submucosal/intramural fibroids	<ul style="list-style-type: none"> <li>Offer the 52 mg LNG-IUD (if submucosal &lt; 3 cm and cavity &lt; 10 cm)</li> <li>Trial an increase in the MP dose</li> <li>Switch to a synthetic progestogen or give additional progestogens</li> <li>Consider resection if submucosal and progestogen adjustments are not acceptable or prevents LNG-IUD insertion</li> <li>Reduce to a lower dose estrogen preparation and supplement with non-hormonal options if required.</li> </ul>

Problem	Potential adjustment
BMI ≥ 30	<ul style="list-style-type: none"> <li>Offer weight management strategies</li> <li>Offer the 52 mg LNG-IUD</li> <li>Increase MP to 200 mg continuous or 300 mg sequential</li> <li>Reduce to a lower dose estrogen preparation and supplement with non-hormonal options if required.</li> </ul>
Perimenopausal and unscheduled bleeding with sHRT	<ul style="list-style-type: none"> <li>Desogestrel can suppress endogenous ovarian activity</li> <li>If &lt; 50 and low thrombotic (VTE) risk, consider switching HRT to a COC</li> <li>Change to an oral preparation (if BMI &lt; 30 and low risk of VTE)</li> <li>Offer the 52 mg LNG-IUD</li> <li>Increase the MP dose or change to a synthetic progestogen</li> <li>3-month trial of an additional progestogen on top of the current preparation</li> <li>Reduce the estrogen dose and offer non-hormonal alternatives.</li> </ul>
Unscheduled bleeding with ccHRT	<ul style="list-style-type: none"> <li>Change to an oral preparation (if BMI &lt; 30 and low risk of VTE)</li> <li>Offer the 52 mg LNG-IUD</li> <li>Increase the MP dose or change to a synthetic progestogen</li> <li>3-month trial of an additional progestogen on top of the current preparation (including women already using a 52 mg LNG-IUD)</li> <li>Consider a 6-month trial of sHRT if recently postmenopausal</li> <li>Reduce the estrogen dose and offer non-hormonal alternatives.</li> </ul>

### Surgical options

- Hysteroscopic myomectomy
- Endometrial ablation
- Hysterectomy

[Click](#) for further information on surgical options.

## Case study – Dawn

- Dawn - 67
- Vulval and vaginal soreness, itching
- Urgency and some leakage (also with cough), nocturia, awareness of bulge
- Has tried 10mcg estradiol pessaries vaginally/0.1% estriol cream
  - both associated with headaches, nausea and breast tenderness
- PMH – hypertension, normal cystoscopy, para 2 (both vaginal deliveries)
- DH – candesartan 12mg, atorvastatin 10mg

BMI 34.6, BP 140/80, non-smoker, no alcohol

Examination:

Cystocoele, descent to introitus with strain  
Marked atrophy, no fissures, no pallor/ulceration

What would you do next?



## Case study – Dawn

- Referred for pelvic floor physiotherapy
- Ring pessary fitting to manage prolapse
- Alternative topical estrogen prescribed
  - 0.005% estriol gel – every other night for 3 weeks then twice weekly  
(as side effects with frequent application of more potent topical estrogen)

## Case study – Melinda

- 60 yr old, marketing consultant
- PMH - Hypertension, ex-smoker (stopped 15 yrs ago), BMI 29
- DH - Candesartan 4mg daily (BP readings normal)
- FHx – Dad had MI at 63, Paternal grandmother stroke at 74
- Started oral sequential HRT (Elleste Duet 1mg) at 55, monthly bleeds, symptoms well controlled
- Changed to oral continuous combined HRT by GP (Elleste Duet Conti) at 59, amenorrhoea at 3-month review

But... clinic BP 154/96 (home readings average 150/90)

GP advised to stop HRT as BP high – intrusive vasomotor symptoms, insomnia, joint pains

What should we do?

## Case study – Melinda

### *Would you?*

- 1) Manage with non-hormonal options?
- 2) Optimise blood pressure and change HRT?

Blood results all normal, Q-risk 9.2%

- Candesartan increased to 8mg daily
- Discussed risks/benefits of HRT, consider transdermal estrogen + progestogen
- Evorel Conti commenced, 1 patch twice weekly

At 3/12 review:

- BP 130/78
- Symptoms improved, small amount of spotting 4 weeks after starting patches, no further bleeding



## Case study – Francis

- 56 yr old
- LMP 2 yrs ago
- FHx osteoporosis prompted discussion with menopause specialist
- Occasional night sweats, anxiety, low libido
- PMH- nil, DH – nil, takes 1000iu vitamin D daily
- FHx
  - Mother, maternal aunt and 3 old sisters all have osteoporosis
  - Mum fractured her hip at 74
- BMI 22.9, BP 130/74, non-smoker, alcohol <10 u per week

What would you do next?



# Case study – Francis

FRAX 10 yr probability of fracture – major osteoporotic 9.4%, hip 0.8%  
 NOGG advises measuring bone mineral density (DEXA)



## Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **UK** Name/ID:  [About the risk factors](#)

**Questionnaire:**

1. Age (between 40 and 90 years) or Date of Birth  
 Age:  Y:  M:  D:

2. Sex  Male  Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture  No  Yes

6. Parent Fractured Hip  No  Yes

7. Current Smoking  No  Yes

8. Glucocorticoids  No  Yes

9. Rheumatoid arthritis  No  Yes

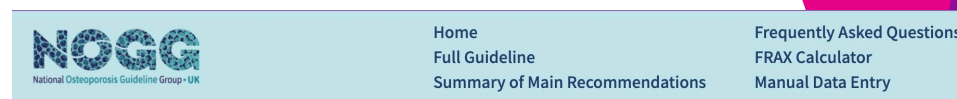
10. Secondary osteoporosis  No  Yes

11. Alcohol 3 or more units/day  No  Yes

12. Femoral neck BMD (g/cm<sup>2</sup>)  
 Select BMD

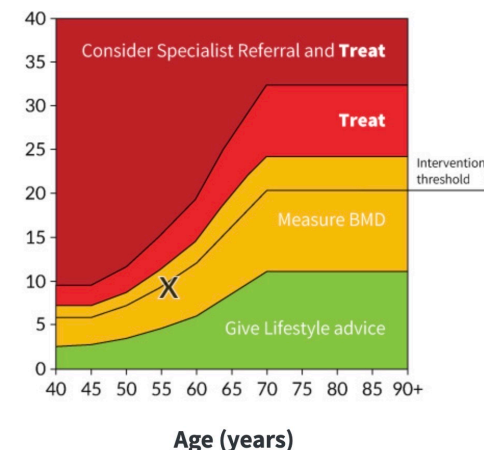
**BMI: 22.9**  
 The ten year probability of fracture (%)

without BMD	
Major osteoporotic	<b>9.4</b>
Hip Fracture	<b>0.8</b>



## Intervention Thresholds

(%) 10-year probability of Major Osteoporotic Fracture





# Case study – Francis

- Commenced Alendronic acid
- Estradiol gel 2 pumps daily and micronized progesterone 100mg daily
- Symptoms improved
- Bone density improved

<https://theros.org.uk/risk-checker/>



[DONATE](#) [JOIN US](#)

## Osteoporosis risk checker

Average completion time: 3 mins.

Take our osteoporosis risk checker and get a personalised report on your bone health.

Osteoporosis is a condition where bones lose strength and become more likely to break. Over 3.5 million people in the UK are currently living with the condition.

It's never too early or too late to start looking after your bones.

Our risk checker is not designed for people who have already been diagnosed with osteoporosis or had their bone health assessed by a healthcare professional.

[START](#)

## DEXA 02/22

Region	BMD (g/cm <sup>2</sup> )	T-score	Z-score
Classification			
AP Spine(L3, L4)	0.829	-2.5	-1.3
Osteoporosis			
Femoral Neck(Left)	0.663	-1.7	-0.6
Osteopenia			
Total Hip(Left)	0.729	-1.7	-1.0
Osteopenia			

World Health Organization criteria for BMD impression classify patients as Normal (T-score at or above -1.0), Osteopenia (T-score between -1.0 and -2.5), or Osteoporosis (T-score at or below -2.5).

## DEXA 03/24

Region	BMD (g/cm <sup>2</sup> )	T-Score
Z-Score		
Classification		
AP Spine (L3, L4)	0.898	-1.8
-0.5		
Osteopenia		
Femoral Neck (Left)	0.675	-1.6
-0.4		
Osteopenia		
Total Hip (Left)	0.756	-1.5
-0.7		
Osteopenia		



Lunch 1230-1330



## Overview of this afternoon

- 1330 - 1450 Menopause masterclass – navigating complexities
  - your questions answered
- 1450 - 1510 Break
- 1510 – 1630 Menopause masterclass
  - case-based discussions
  - time for questions



# Menopause masterclass - navigating complexities

- Migraine
- Epilepsy
- New guidance
- Menopause and autism/ADHD
- Menopause and cancer (hormonal and non-hormonal treatment options)
- Progestogens (cancer risk choice, prescribing, off label medications)
- Vegan/vegetarian options

# Migraine

- Is it migraine? Yes to at least two of the following, migraine is likely.

Photophobia	Does light bother her when she has a headache?
Impairment	Does she experience headaches that impair ability to function?
Nausea	Does she feel nauseated with a headache?

- Is it migraine with aura? Yes to all three, migraine aura likely.

Does she have visual disturbance that:

Starts before the headache	Lasts up to an hour	Resolves before the headache
----------------------------	---------------------	------------------------------

- Fluctuations in estrogen and menstrual disturbance increase migraine prevalence in perimenopause
- Effective management of symptoms can improve migraine

# Migraine

- Perimenopausal women with no migraine aura can benefit from COCP until age 50
- Migraine aura does not contraindicate HRT
- Existing migraine with aura
  - Use transdermal estrogen
  - Start with low dose and titrate to address symptoms (patch can often be better)
  - Continuous combined often superior migraine control (consider IUS)
- New onset migraine with aura
  - Exclude TIA
  - Change from oral estrogen to transdermal
  - Use lowest effective dose to control symptoms
  - Consider non-hormonal options if symptoms not resolving/migraine frequency increases

# Epilepsy

- Epilepsy can be affected by hormone changes during perimenopause
  - 40% women have more seizures just before/during menstruation
- ‘catamenial’ epilepsy, this can improve after menopause
- Women with frequent seizures reach menopause around 3-5 years earlier than average
- Some antiepileptics can affect vitamin D and hence bone density
- Lifestyle optimisation is key
- Avoid seizure triggers such as sleep deprivation, alcohol
- HRT can be used in women who are epileptic but epilepsy should be monitoring when starting/changing HRT in case antiepileptic medication needs adjusting

## Epilepsy – management options

- Very little research undertaken on HRT in women with epilepsy
- CEE +MPA demonstrated increased seizure frequency
- Safest option is transdermal estrogen with micronized progesterone, vaginal oestrogen fine
- Estrogen generally considered to increase seizure risk but progesterone may reduce seizure effects through the effect on GABA
- Some antiepileptics interact with HRT reducing HRT efficacy (may need a higher dose) - carbamazepine, phenobarbital, phenytoin, primidone, topiramate (and more)
  - Oral > transdermal.
- Those that do not affect HRT include clonazepam, ethosuximide, gabapentin, lamotrigine, levetiracetam, sodium valproate and others
- Lamotrigine – HRT can decrease lamotrigine blood levels

## Use of incretin-based therapies in women using hormone replacement therapy (HRT)

### Introduction

Incretin-based therapies refers to a class of medications used for the treatment of diabetes and obesity that mimic the action of incretins — “gut hormones” that regulate insulin secretion, appetite and satiety, amongst other functions.

This BMS Tool for Clinicians will clarify:

- Background information about obesity and diabetes, the primary disease indications for incretin-based therapies
- Indications for the use of incretin-based therapies
- Considerations when prescribing incretin-based therapies in women using HRT during the menopause transition and post-menopause
- General guidance

This Tool for Clinicians will not cover all the effects of incretin-based therapies or their potential effects if used outside regulator approved indications.

### Background

Rates of obesity have more than trebled in the UK over the last 30 years in line with the worldwide obesity epidemic<sup>1</sup>. Complex environmental factors contribute to this increase and the World Health Organisation has shifted the focus from individual to societal causes.

According to NHS digital data from 2022, the proportion of overweight and obesity combined among women aged 45 to 54 was 64% with the rate of obesity being 34%. Rates among women aged 55 to 64 were 60% and 35% respectively.

A pragmatic approach to adjusting progesterone dosing with different HRT preparations, based on limited available evidence, is summarised in box below:

Current progestogen	Recommendation
Combined patch	No change
LNG-IUD up to 5 years	No change
Oral progestogen/progesterone*	Consider changing to LNG-IUD/increase dose of progestogen/progesterone at initiation for 4 weeks and maintain higher dose for 4 weeks after any dose increment
Vaginal progesterone (off licence)	No change

\* Weight loss injections may reduce the effectiveness of oral HRT medications. Review of current HRT is recommended while using these medications.

<https://thebms.org.uk/wp-content/uploads/2025/05/23-BMS-TfC-Use-of-incretin-based-therapies-APRIL2025-E.pdf>



## Measuring estradiol levels

- Measuring a serum estradiol does not reflect all estrogenic activity.
- Assays do not differentiate between endogenous and exogenous estradiol, active and inactive SHBG bound estradiol.
- There is a wide range of 'normal' estradiol values
- Measuring a serum estradiol level is particularly unhelpful in patients taking oral estradiol as the main circulatory metabolite is estrone
- There is a correlation between serum estradiol and clinical effect within a threshold level for estradiol
- The serum level in an individual woman does not predict therapeutic effect
- There is a dose-related impact of HRT on bone density, but there is no clear lower threshold (benefit has been demonstrated at low estradiol doses and low systemic estradiol levels)
- The upper limit of estradiol may vary between individuals in terms of tachyphylaxis and there is a lack of data to inform any threshold in terms of risk
- Monitoring serum estradiol may be useful in monitoring women with female hypogonadism including POI, but a holistic approach is necessary to ensure adequate treatment

1 of 13

BMS Tool for Clinicians  
Measurement of serum estradiol  
in the menopause transition



Measurement of serum estradiol  
in the menopause transition



## Menopause and autism

Menopause may present additional challenges:

- Greater impact of hormonal changes
- Increased sensory sensitivity to symptoms

(can be exacerbated in menopause when physical symptoms and coping provides an additional challenge)

- Increased risk of mental health issues  
(including co-existing mental health issues)
- Increased burden of physical health symptoms

- Reduced access to medical support/difficult relationships with HCPs

(lack of rapport, difficulty in communication, HCPs not recognising atypical presentations/description of symptoms)

Original Article



**“A perfect storm”: Autistic experiences of menopause and midlife**

Miranda J Brady<sup>1</sup>, Christine A Jenkins<sup>2</sup>,  
Julie M Gamble-Turner<sup>3</sup>, Rachel L Moseley<sup>1</sup>,  
Margaret Janse van Rensburg<sup>1</sup> and Rose J Matthews<sup>4</sup>

Autism  
1–14  
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DOI: 10.1177/1362261224124458  
journals.sagepub.com/home/aut





Common themes in both autistic and non-autistic women but some variability:

1) Information about menopause

- Type of information required, information can be scare-mongering (facts needed)
- Withdraw from social support, find it difficult to communicate (even when social support present)

2) Experiences of menopause

- Challenges associated with change and unpredictability
- More emotions around periods stopping/not realising what was happening, uncertainly about how they would feel
- Difficulty describing physical symptoms as easily/as well
- (increases challenges for HCPs in recognising symptoms as related to menopause)
- Lack of predictability e.g. when a flush may occur more challenging

Journal of Health Psychology

Impact Factor: 2.2 / 5-Year Impact Factor: 2.9

Journal

Open access | Research article | First published online February 15, 2025

Common and unique menopause experiences among autistic and non-autistic people: A qualitative study

Martha A Piper and Rebecca A Charlton | View all authors and affiliations

OnlineFirst | <https://doi.org/10.1177/13591053251316500>

3) Medical support for menopause

- Barriers to access – making appts, using telephones
- HCPs not accommodating autistic differences
- Lack of trust in HCPs

‘autistic people are automatically on the hypochondriac list at the GP’

4) Menopause alongside other issues

- Lifelong experiences impact more at menopause in autistic people
- Autism ‘mask’, trying to hide their diagnosis and menopause then provided an additional challenge (a ‘menopause mask’ on top of the autistic one)



## ADHD and menopause

### Why do we know so little?

- Focus on ADHD as male disorder (aspects related to adult women (e.g. changes during hormonal changes) understudied)
- Many studies ask no/few questions about menopause (often only ask about age of menopause not symptoms)
- Many population-based studies don't ask about ADHD symptoms in adulthood
- Registry studies that record ADHD diagnosis may not record menopause symptoms
- Lack of biomarkers (no test to diagnose ADHD or menopause) – more self-reported

### Why do women with ADHD have more issues at menopause?

- Dopamine has a key role in ADHD (stimulants reduce dopamine reuptake)
- Oestrogen can affect dopamine availability (reduced E2 could result in lower dopamine availability)
- Higher risk of hormonal sensitivity, greater exacerbations across the menstrual cycle
- Women with ADHD more likely to have PMDD (Dorani 2021)
- Genetic evidence suggest links between ADHD and menopause (age at menopause) but could be compounded by other factors e.g. smoking, age at first child



## ADHD and menopause

### What are women telling us?

- ADHD can become more prominent in menopause, symptoms can be more intense
  - Reader survey from ADDitude magazine (1500 people)
- 94% respondents said menopause made ADHD symptoms worsen  
>50% menopause was a time when ADHD symptoms most impacted their life

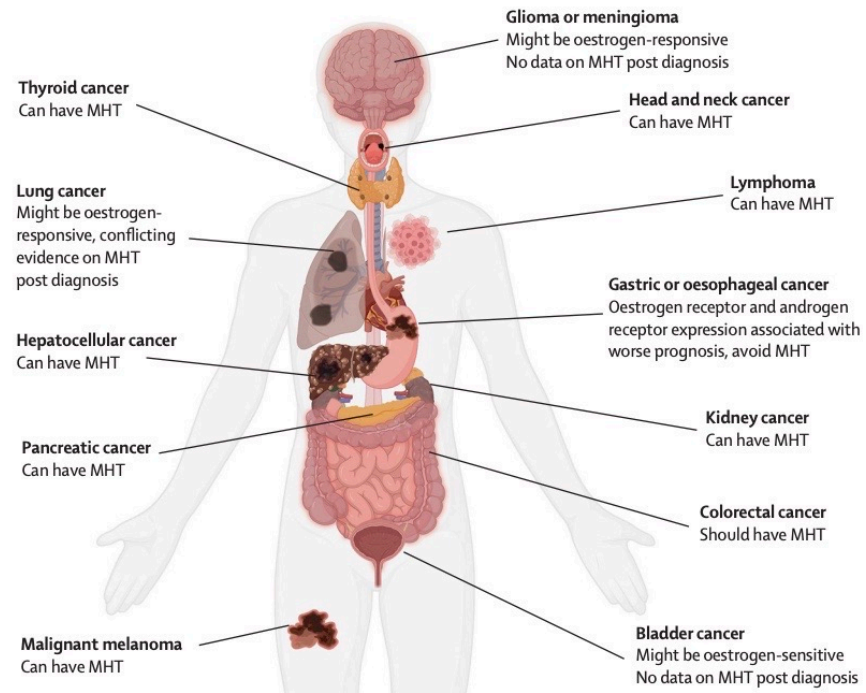
### What does the data show?

- Women >40 - rate of diagnosis not increasing compared with other age groups (2022 data)
- One quantitative surgery (Dorani 2021) – more menopause symptoms on Greene Climacteric scale reported in peri/menopausal in women with ADHD
- Childhood ADHD diagnosis – higher incidence of 'reported' menopause symptoms in later life

### Remaining questions

- Do women with ADHD experience more, different or severe symptoms in menopause?
- Do women with ADHD respond differently to HRT?
- How do we distinguish ADHD symptoms to menopause? – can be difficult e.g. brain fog, mood change, poor concentration

# HRT after cancer



The Lancet 2024: 403; 984-996

**Table 1: Summary of recommendations for use of systemic HRT and vaginal estrogen following treatment of gynaecological cancer**

Primary Cancer	Subtype or Risk Group	Systemic HRT	Vaginal Estrogen
Ovarian Fallopian tube Primary peritoneal	High grade serous	Yellow	Green
	Low grade serous stage 1	Green	Green
	Low grade serous stage 2+	Red	Yellow
	Endometrioid stage 1	Green	Green
	Endometrioid stage 2+	Yellow	Green
	Clear cell	Green	Green
	Mucinous	Green	Green
	Granulosa cell stage 1	Yellow	Green
	Granulosa cell stage 2+	Red	Yellow
	Germ Cell	Green	Green
Endometrial	Borderline tumour: No residual disease	Green	Green
	Borderline tumour: Peritoneal implants, microinvasive disease, residual disease, recurrence	Yellow	Green
	Low and intermediate risk	Green	Green
	High-intermediate risk	Yellow	Yellow
	High risk: ER/PR negative	Red	Yellow
Cervical	High risk: ER/PR positive	Red	Yellow
	Advanced and metastatic	Red	Yellow
Cervical	All	Green	Green
Vulval	All	Green	Green
Vaginal	All	Green	Green
Uterine sarcoma	Leiomyosarcoma	Red	Red
	Endometrial stromal sarcoma	Red	Red

Green	Benefits usually outweigh risks. Suitable for non-specialist use.
Yellow	Refer to text of BGCS/BMS guidelines. Discuss benefits and risks for the individual patient. Consider specialist advice.
Red	Not recommended. Refer for specialist advice if non-hormonal approaches are not effective.

**BGCS/BMS**  
Guidelines on Management of Menopausal Symptoms after Gynaecological Cancer

## Women with an increased risk of breast cancer

- The majority of women have a low lifetime risk of breast cancer
- No strong evidence to suggest HRT has an additive effect upon risk of diagnosis for those with a family history or personal diagnosis of a high-risk benign breast condition
- Risk conferred will depend on the baseline risk in higher risk women
- It is recommended to avoid HRT in women at high risk, with the exception of BRCA mutation carriers who have had prophylactic oophorectomy (HRT use in these cases until the age of 50 is not associated with an increased risk for breast cancer)
- In BRCA carriers – use non-hormonal options/lifestyle management
- High risk symptomatic women should have menopause specialist input

<https://www.canrisk.org/>



## Women with a history of malignancy

- Counsel women about the risk of early menopause and the symptoms associated with certain cancer treatment
- Offer specialist menopause referral
- If severe, refractory symptoms offer HRT but vital to document informed consent  
(but not those using aromatase inhibitors)
- HABITS RCT (not placebo controlled, 442 women)
  - terminated early after 2 yrs follow-up, increased risk of recurrence
- Stockholm trial (RCT, 378 women)
  - terminated after HABITS results reported
  - no excess risk of recurrence after 4.1yrs f/up
  - no difference in recurrence after 10.8yrs f/up
  - significantly higher numbers of contralateral breast cancers in HRT arm

## Breast cancer: summary

- Based on current evidence:

A history of invasive breast cancer should c/i HRT

- increased risk of recurrence with ER positive disease
  - ER –ve – up to 30% contralateral primaries are ER +ve
  - ER –ve - up to 8% distant metastases are ER +ve
- No data on risk of recurrence after DCIS



## Non-hormonal treatment options

Some have significant impact on frequency and severity of VMS

- Clonidine - 50-100mcg bd
- Venlafaxine - 37.5-75mg daily
- Oxybutynin - 2.5-5mg od-bd
- SSRIs - Paroxetine 10mg od, Citalopram 10/20mg, Fluoxetine 10/20mg (c/i with Tamoxifen)
- CBT – mood, sleep, physical symptoms
- Neurokinin 3 receptor antagonists



## Neurokinin 3 Receptor Antagonists

- MHRA licenced Veoza in UK end of 2023 (NICE – not yet included in guidance)
- HIGHLIGHT - phase 3 clinical trial, Veoza in women with PMH breast cancer using endocrine therapies underway
- Elinzanetant - Neurokinin 1 and 3 receptor antagonist
  - Trials (OASIS 1-4) showed reduction in moderate to severe VMS and improved sleep and QOL
  - OASIS 4 – Phase 3, focused on breast cancer patients with VMS due to endocrine therapies (Tamoxifen/AIs)
  - MHRA licenced Lynkuet in July 2025 – currently no supply in UK for private use

# Topical estrogen after breast cancer

- Cohort study (50,000 woman) with breast cancer diagnosis
  - no increase in early breast cancer specific mortality with vaginal estrogen therapy (study did not look at recurrence in women using AIs)<sup>1</sup>
- Observational Danish study reported an increase in recurrence of breast cancer in women using vaginal estrogen and an AI<sup>2</sup>
- DHEA – converted to estrogens and androgens in the vaginal epithelial cells
- Ospemifene – SERM, agonist in vaginal mucosa, lowers vaginal pH, improves VMI (antagonist on breast/endometrial tissue) 60mg once daily orally
- Vaginal laser – CO<sub>2</sub> (microablative) or Erbium Yag laser (non-ablative)– show benefit – improves blood supply and induces collagen remodelling

1. Nappi RE, et al. Climacteric. 2016;19(2):188-97
2. Tan O, et al. Menopause. 2012 Jan;19(1):109-17
3. BMS Consensus Statement Genitourinary Syndrome of Menopause Nov 2025

## Topical estrogen after breast cancer

### In summary

- Non-hormonal treatments advocated –
  - lubricants, moisturisers, emollients, vulval skin care
- PMH breast cancer with no current treatment
  - can use topical estrogen
- PMH breast cancer using Tamoxifen
  - can use topical estrogen therapy
- PMH breast cancer on AI
  - ? switch to Tamoxifen and consider topical estrogen therapy
  - Drug holiday
  - Joint discussion with oncology if wishes to consider topical estrogen while using AI



# What about testosterone after breast cancer?

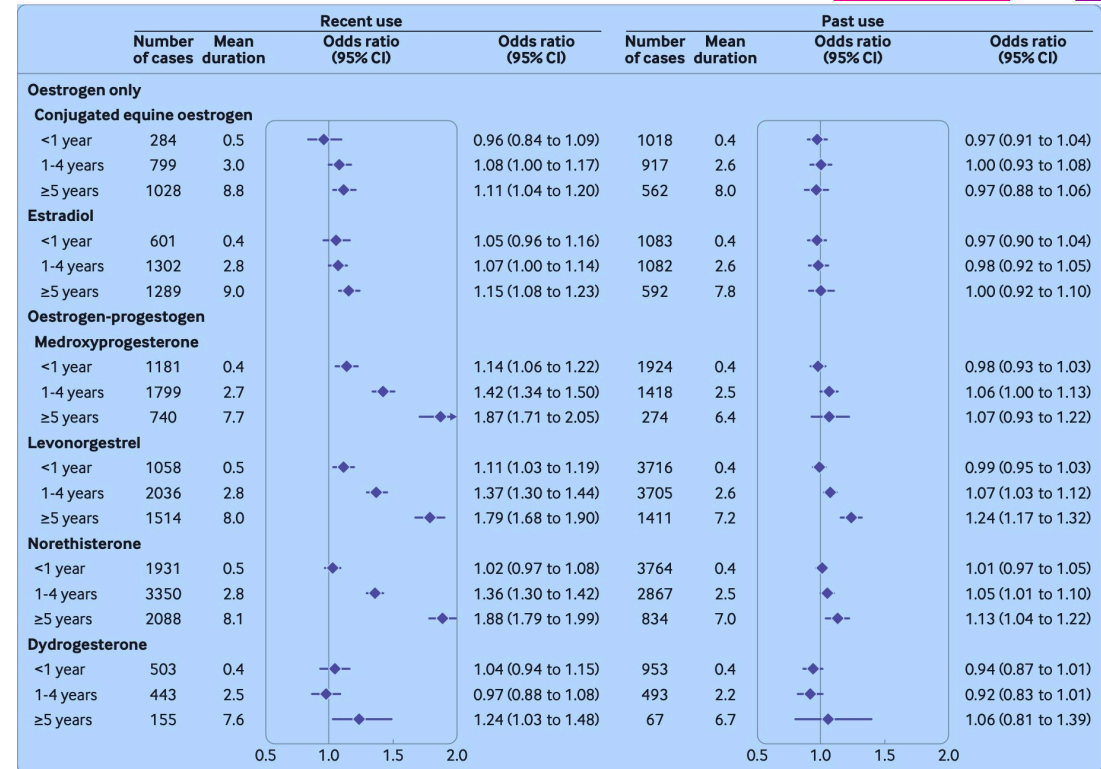
- NICE (NG23) and BMS recommend a trial of conventional HRT is given before considering testosterone supplementation
- In women not using concomitant estrogen containing HRT the incidence of adverse androgenic side effects was greater
- Peripheral aromatisation of testosterone to estrogen elevating serum estradiol is a concern
- One study evaluated testosterone in women with ER positive breast cancer on AI – estradiol levels remained  $<2.7\text{pg/mol}$  and improvement in sexual function index (small trial, 22 patients)<sup>1</sup>



## Progestogens and cancer risk

- Estrogen plus micronized progesterone – no significant increase in breast cancer risk for up to 5 years use (HR 1.11)
- Estrogen plus micronized progesterone - >5 years associated with a small increase in breast cancer risk (HR 1.31)
- LNG-IUS plus estrogen - similar risk to regimens containing oral progestogens

E3N cohort study, Fournier et al (2014) ; Finnish Cancer Registry



Vinogradova, *BMJ* 2020;371:m3873

# Progestogen choices

- Progestogens – natural progesterone, dydrogesterone and synthetic compounds
- All derived from progesterone, testosterone or spironolactone

Retroprogesterone

Progesterone derivatives

Testosterone derivatives

Spironolactone derivatives

Dydrogesterone (Femoston/Nalveen)

Medroxyprogesterone acetate

Nomogestrol acetate (Zoely)

Desogestrel

Dienogest (Qlaira)

Levonorgestrel (52mg LNG-IUD)

Norethisterone acetate

Tibolone

Drospirenone (Slynd)

## Progestogens - doses

**Table 3: Progestogen dose per licensed estrogen dose in the baseline population**

Estrogen dose	Micronised Progesterone		Medroxy progesterone		Norethisterone		LNG-IUD (52mg)
	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
Standard	100 mg	200 mg	2.5-5 mg	10 mg	5 mg*	5 mg*	
Moderate	100 mg	200 mg	5 mg	10 mg	5 mg	5 mg	
High	200 mg	300 mg	10 mg <sup>^</sup>	20 mg <sup>^</sup>	5 mg	5 mg	

\* 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).

<sup>^</sup> 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.

# Progestogens – continuous combined

- Combined oral preparation
- Combined transdermal patch
- Oral/transdermal estradiol + separate progestogen



BMS Tools for Clinicians – HRT preparations and equivalent alternatives.  
Jan 2024.

## Progestogen:

**Micronised Progesterone: Utrogestan 100mg** orally at night daily on continuous basis

Or **Provera a minimum of 2.5mg** orally daily on continuous basis

Or **Norethisterone 5mg** orally daily on continuous basis (1mg would be sufficient for use in a continuous combined regimen but not available in stand-alone preparations)

**Off license use of norethisterone in progestogen only contraceptive pills** (e.g. **Noriday** 3 x tablets of 350 micrograms a day, will provide 1.05mg of norethisterone) may be considered as an equivalent alternative.

Or **52mg Levonorgestrel IUD**

Or **Drospirenone 4 mg (Slynd)** 1 active hormonal tablet 4 mg can be taken daily on a continuous basis (omitting the 4 hormone free pills in the pack)

Off licence use of this progestogen-only contraceptive pill can be considered as an equivalent alternative for women experiencing progestogenic side effects with other preparations.

Earlier studies have reported that desogestrel 150 micrograms is effective as the progestogen component of HRT with no increase in the risk of endometrial hyperplasia. There is lack of evidence on the use of desogestrel 75 micrograms as the progestogen component of HRT.

If desogestrel 75 micrograms is used as contraception in women receiving HRT, it would be recommended to add further progestogen (e.g. Utrogestan 100 mg daily or 200 mg for 12 days a month) to provide adequate endometrial protection.



# Progestogens – sequential combined

- Combined sequential oral preparation
- Combined sequential transdermal patch
- Oral/transdermal estradiol + separate sequential progestogen



## Progestogen:

**Micronised Progesterone: Utrogestan 200mg orally for 12 days a month at night (cyclical)**

**Or Provera 10mg orally for 12 days a month**

**Or Norethisterone 5mg orally for 12 days a month**

**Or 52mg Levonorgestrel IUD**

BMS Tools for Clinicians – HRT preparations and equivalent alternatives.  
Jan 2024.



# New/off label options/cautions

## Off label use:

- Micronised progesterone vaginally – same dose as oral (cyclical/continuous)
- Noriday 3x 350mcg daily
- 2xDesogestrel daily (150mcg daily)
- Slynd – 4mg Drospirenone daily (omit the green placebo pills each packet)

Precedent set from Angeliq 0.5/1mg and 1/2mg oral combined HRT

- 13.5mg and 19.5mg LNG-IUS – use additional licenced progestogen
- Nalvee (dydrogesterone) 10mg tablets

**Hormone replacement therapy:** i.e. as supplement in estrogen treatment in non-hysterectomised women with symptoms due to natural onset of or surgically induced menopause:

- Continuous sequential therapy: continuous use of an estrogen; sequential supplementation of 10 mg dydrogesterone during the last 14 days of each 28-day cycle

??

- Cyclical treatment: cyclic use of an estrogen with a treatment-free period, usually 21 days on and 7 days off treatment. For the last 12-14 days of estrogen use, 10 mg of dydrogesterone is supplemented.

- Depending on the clinical response, the dosage may be adjusted to 20 mg dydrogesterone daily in the course of the treatment.



## Vegan/vegetarian options

### OESTROGEN

- ORAL
  - No vegan estrogen-only oral tablets
  - Lactose containing estrogen-only tablets – Elleste Solo, Zumenon, Prodynova
  - Combined oral preparations containing animal products (gelatin) - Indivina, Tridestra, Bijuve
  - Premarin/Prempak and Premique – contains estrogen derived from horses
- TRANSDERMAL
  - Gels - Oestrogel, Sandrena suitable for vegan and vegetarian
  - Patches - Evorel, Estraderm MS, Estradot, Prodynova TS, Femseven suitable for vegan and vegetarian
- VAGINAL
  - Ovestin, Imvaggis, E-string, Intrarosa – no animal products
  - Vagifem, Vagirux contain lactose

### PROGESTOGEN

- ORAL/VAGINAL
  - Micronised progesterones  
Utrogestan and Gepretix contain bovine gelatin  
Gepretix certified as halal/kosher  
Cyclogest pessaries and Crinone gel suitable for vegans
  - Lutigest – contains lactose, no gelatin
  - Provera, Norethisterone contain lactose

### INTRAUTERINE

- Mirena IUS – inserter contains animal products
- Benilexa/Levosert fine for vegans

### TESTOSTERONE

- Tostran, Testogel, Testim and Androfeme suitable for vegan and vegetarian



Quick break....  
1450-1510



## Case study - Elizabeth

- 47 years old
- Fatigue, brain fog, irritability, low libido, headaches, joint pains
- Monthly bleeds but heavy, clots, iron deficiency anaemia
- Previous copper IUD (removed at expiry), using condoms
- PMH – migraine aura, mild asthma
- DH – salbutamol prn, ferrous fumarate
- FHx – Mother - hypertension and breast cancer (diagnosed at 58)
- BP 103/63, BMI 20, non-smoker, alcohol 3 units/week

What would you do next?

## Case study - Elizabeth

<https://cks.nice.org.uk/topics/menorrhagia-heavy-menstrual-bleeding/management/management/>

- **For women with menorrhagia and no identified pathology; fibroids less than 3 cm in diameter, which are not causing distortion of the uterine cavity; or suspected or diagnosed adenomyosis:**
  - Consider a levonorgestrel intrauterine system (LNG-IUS) as the first-line treatment.

Examination: Normal cervical appearance, no masses

Pelvic USS: Heterogeneous myometrium? Adenomyosis/fibroid change  
2.1cm intramural fibroid right posterior wall  
8mm endometrium, normal ovarian appearances



## HRT is not a contraceptive<sup>1</sup>

- If aged less than 50 years: needs contraception for 2 years after her LMP
- If aged 50 years or older: needs contraception for 1 year after her LMP
- Women can continue using hormonal contraception until the age of 55 years, at which point spontaneous conception is *‘exceptionally uncommon’*

**Table 9: Contraceptive options in conjunction with hormone replacement therapy (HRT)**

Contraceptive method	Safety with HRT	Role in HRT	
		Women aged <50	Women aged ≥50
<b>52mg Levonorgestrel intrauterine system (LNG-IUS)</b>	Safe to use as contraception alongside estrogen of choice.	A 52mg LNG-IUS may be used up to 5 years for endometrial protection and needs to be replaced regularly when used for this purpose, regardless of age at insertion.	
<b>Progestogen-only injectable (DMPA)</b>	Safe to use as contraception alongside sequential HRT but consider change to lower-dose progestogen-only method.	Highly likely to be effective for endometrial protection with estrogen as part of HRT but cannot be recommended as unlicensed for this indication.	
<b>Progestogen-only implant (IMP)</b>	Safe to use as contraception alongside sequential HRT.	Cannot be recommended at the present time for endometrial protection as part of HRT as no evidence to support efficacy.	
<b>Progestogen-only pill (POP)</b>	Safe to use as contraception alongside sequential HRT.	Cannot be recommended at the present time for endometrial protection as part of HRT as no evidence to support efficacy.	
<b>Combined hormonal contraception (CHC)</b>	Do not use in combination with HRT.	Can be used in eligible women <50 as an alternative to HRT.	Women should be advised to switch to a progestogen-only method of contraception at age 50; see above for alternative options as they relate to HRT.

1. Faculty of Sexual & Reproductive Healthcare. Contraception for women aged over 40 years. FSRH, 2017. Available at: [www.fsrh.org/standards-and-guidance/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/](http://www.fsrh.org/standards-and-guidance/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/)



## Case study - Elizabeth

What did I do?

- LNG-IUS fitted
- Commenced estradiol 50mcg patch twice weekly and titrated to control symptoms
  
- Increased to 75mcg estradiol patch twice weekly with 52mg LNG-IUS
- Some irregular bleeding initially
- Review at 6 months
  - bleeding minimal (occasional brown spotting only)
  - Hb stable
  - symptoms well controlled
  - libido improved



## Case study – Marianne

- 53 on HRT for 9/12
  - presented initially with achy joints, insomnia, anxiety, night sweats, vaginal dryness low libido, impaired orgasm, dyspareunia
- PMH – hypothyroidism (levothyroxine 75mcg daily), asthma (luforbec and salbutamol)
- NKDA
- FHx – stroke in paternal grandfather, Alzheimer’s maternal grandmother
- Ex-smoker, no alcohol
- BP 130/80, BMI 32.9 (was 36.3 at first consultation)

### Current HRT

- Estradiol 75mcg patch
- Micronised progesterone 200mg daily (amenorrhoea)
- Vagirux twice weekly (initial loading dose nightly 2/52)

## When should I consider testosterone?

- No need to replace purely if levels are low
- Adopt a biopsychosocial approach
  - relationship issues
  - physical issues e.g. vulvo-vaginal atrophy
  - psychological issues
  - medication e.g. SSRIs/SNRIs
- Limited data for testosterone replacement in premenopausal women
- NICE (NG23) and the BMS recommend that a trial of conventional HRT is given first
- Oral estrogen (in particular CEE) increases SHBG levels
- Changing women from oral to transdermal estrogen can be beneficial (increases circulating free testosterone)

<https://thebms.org.uk/wp-content/uploads/2022/12/08-BMS-TfC-Testosterone-replacement-in-menopause-DEC2022-A.pdf>

Prof Susan Davis/Marla Shapiro – IMS, you tube



## Testosterone – prescribing and application

- No female licensed preparations in UK, most products used ‘off label’
- Commonly used products
  - Testim gel (50mg/5ml) – 0.5mls daily, one tube lasts 10 days
  - Tostran gel (2% in 60g canister) – 1 pump on alternate days (each pump=10mg) one canister lasts 240 days
  - Testogel (40.5mg/2.5g) – 0.5mls daily, one sachet lasts 8 days
  - Androfeme 1% cream (10mg/ml) – 0.5mls daily = 5mg, one tube lasts 100 days



### Application

- Apply the gel/cream to clean, dry skin (lower abdomen/upper thighs)
- Allow to dry before dressing and avoid skin contact with others
- Wash hands after application
- Avoid washing the area of application for 2-3 hours



## Testosterone – monitoring

- The physiology of testosterone is complex
- Testosterone variably binds to SHBG, albumin and other proteins in blood
- Metabolism happens in target tissues so blood levels are generally a poor
- Total testosterone levels are therefore advised to monitor therapy
- Check total testosterone levels before
- Reassess testosterone levels at 3-6 weeks ideally
- Ongoing monitoring every 6-12 months
  - total testosterone levels and clinical assessment for signs of androgen excess
- Ensure levels remain in normal female physiological range

SHBG can be helpful in the following circumstances

- high SHBG e.g. oral estrogens, can explain lack of response
- low SHBG – side effects despite normal total testosterone levels



## Case study – Marianne

Back to our patient:

- Initial blood tests:

Testosterone - 0.84, SHBG - 63.6

- Started Testogel 40.5mg/2.5g sachets, 1/8<sup>th</sup> sachet daily (12 sachets/3 months)
- Repeat bloods 8/52 after starting – testosterone 1.49

Review – improved libido, arousal, also noticed improved mood and energy  
For ongoing annual review/monitoring with GP in line with shared care agreement

<https://www.bucksoxonberksw.icb.nhs.uk/media/5079/hrt-formulary-and-treatment-guidance.pdf?UNLID=717766772024114134443>



## Case study - Patricia

- 54
- BMI 42, non-smoker, BP normal
- No relevant PMH/FHx, started HRT 2 years ago, dose gradually increased
- Prescribed 2 x 100mcg estradiol patches twice weekly 100mg micronized progesterone daily
- Presents with worsening sweats, anxiety, palpitations and intermittent bleeding (dark blood)
- No new partners, patches adhering well
- Examination: NAD (cervical screening normal previous year) cervical appearance normal

Admits mood change since using HRT so uses 100mg progesterone every other day not daily....



## Case study - Patricia

### Referred under USCP

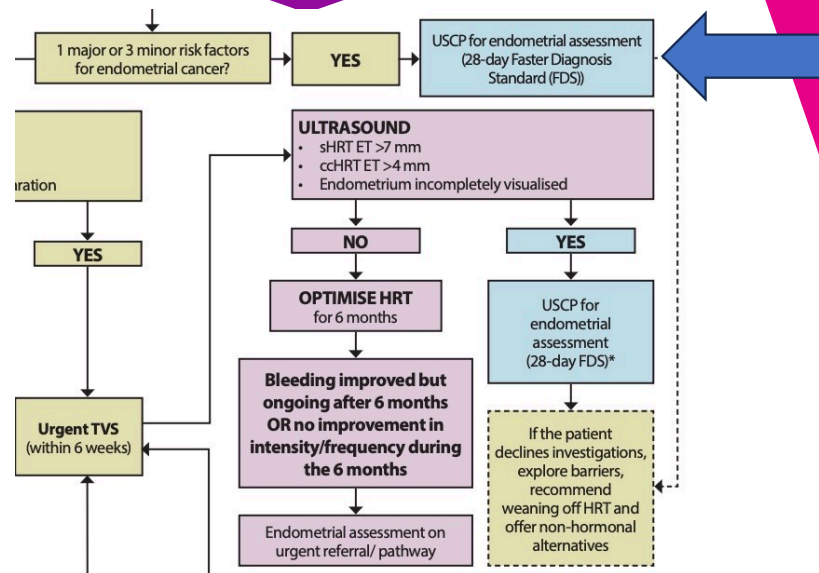
- TV USS
- 18mm endometrium with cystic spaces
- Hysteroscopy/biopsy
- endometrial hyperplasia without atypia
- 52mg LNG-IUS fitted

### HRT adjusted

- Reduced to 100mcg patch twice weekly
- Lifestyle advice

### Review 3/12 post hysteroscopy

- Bleeding reducing
- Anxiety/vasomotor symptoms resolved

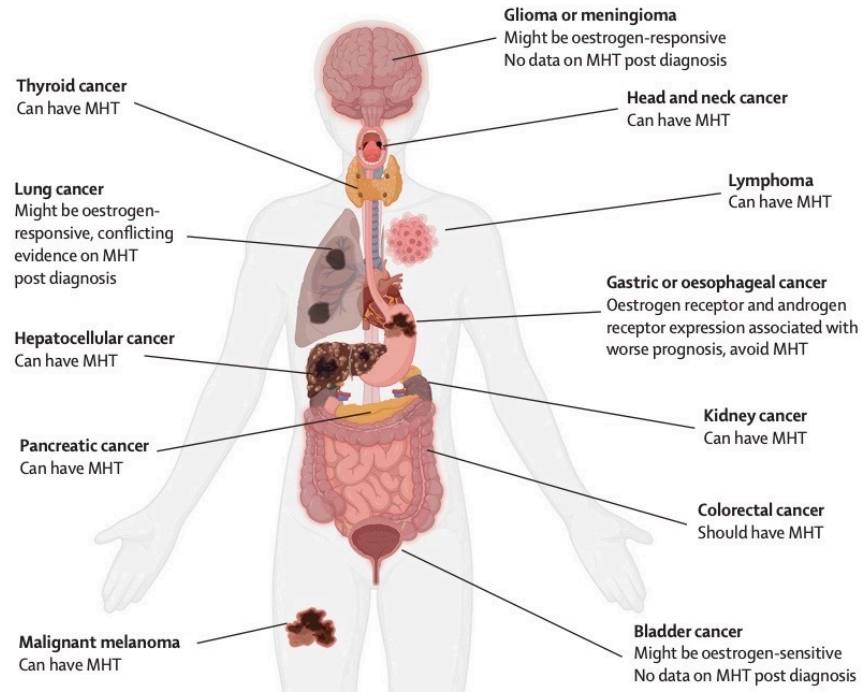


- MAJOR risk factors for endometrial cancer**
- BMI  $\geq$  40
  - Genetic predisposition (Lynch / Cowden syndrome)
  - Estrogen-only HRT for > 6 months in women with a uterus
  - Tricycling HRT (quarterly progestogen) for > 12 months
  - Prolonged sHRT regimen: use for more than 5 years when started 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

## Case study – Vanessa

- 59
- 3-year history of intrusive flushes/sweats, otherwise no other issues
- Always hot, carries a fan with her, soaks her hair
- Affects exercise/social life
- Alcohol 18-24u/week, non-smoker, BMI 30.8
- PMH
  - breast cancer aged 35 (grade 3, ER positive), partial mastectomy, chemo, radiotherapy
  - Tamoxifen for 5yrs, infrequent bleeds until mid 40's then stopped
  - normal bloods this year (ESR/FBC/LFTS/CRP/TFTs)
  - #humerus skiing in 2007
  - psoriasis
- DH – Omeprazole, Secukinumab



The Lancet 2024: 403; 984-996

**Table 1: Summary of recommendations for use of systemic HRT and vaginal estrogen following treatment of gynaecological cancer**

Primary Cancer	Subtype or Risk Group	Systemic HRT	Vaginal Estrogen
Ovarian Fallopian tube Primary peritoneal	High grade serous	Yellow	Green
	Low grade serous stage 1	Green	Green
	Low grade serous stage 2+	Red	Yellow
	Endometrioid stage 1	Green	Green
	Endometrioid stage 2+	Yellow	Green
	Clear cell	Green	Green
	Mucinous	Green	Green
	Granulosa cell stage 1	Yellow	Green
	Granulosa cell stage 2+	Red	Yellow
	Germ Cell	Green	Green
Endometrial	Borderline tumour: No residual disease	Green	Green
	Borderline tumour: Peritoneal implants, microinvasive disease, residual disease, recurrence	Yellow	Green
	Low and intermediate risk	Green	Green
	High-intermediate risk	Yellow	Yellow
	High risk: ER/PR negative	Red	Yellow
Cervical	High risk: ER/PR positive	Red	Yellow
	Advanced and metastatic	Red	Yellow
Cervical	All	Green	Green
Vulval	All	Green	Green
Vaginal	All	Green	Green
Uterine sarcoma	Leiomyosarcoma	Red	Red
	Endometrial stromal sarcoma	Red	Red

Green	Benefits usually outweigh risks. Suitable for non-specialist use.
Yellow	Refer to text of BGCS BMS guidelines. Discuss benefits and risks for the individual patient. Consider specialist advice.
Red	Not recommended. Refer for specialist advice if non-hormonal approaches are not effective.

## BGCS/BMS Guidelines on Management of Menopausal Symptoms after Gynaecological Cancer

## Case study – Vanessa

### **FRAX**

- 9.7% major osteoporotic fracture, 1.4% hip
- DEXA requested, vitamin D/calcium optimisation

### **DEXA**

- T score spine -2.9 (normal femoral neck/hip)
- Alendronic acid 70mg once weekly for 5yrs
- Adcal-D3
- Repeat DEXA in 5 years

### **LIFESTYLE ADVICE**

- minimise alcohol, lower BMI

### Has tried:

- Oxybutynin – urinary retention
- Bumetanide – peripheral neuropathy
- Sertraline/Paroxetine ineffective
- Not tried Clonidine/Gabapentin
- Researched Veoza and wanted to try
- Discussed new therapy, currently only available privately
- LFTs prior to starting normal
- Reviewed after 2/12
  - marked reduction in flushes (severity and frequency)
  - no side effects
  - repeat LFTs at 4 weeks normal

## Case study - Farzana

- 54
- Postmenopausal (LMP aged 49)
- Started HRT age 50
  - estradiol 1mg + dydrogesterone 5mg orally once daily
- Telephone consultation with GP 18 months ago as vulval irritation, discharge
- No bleeding, cervical screening in date, regular male partner (no change)
- Prescribed Clotrimazole 500mg pessary PV and 1% clotrimazole cream
- Minor relief of symptoms but when recurred further telephone call with GP
- Prescribed vaginal estradiol 10mcg pessaries, nightly for 2 weeks then twice weekly thereafter
- Again, minor relief but ongoing itching, soreness pain
- F2F with nurse at GP surgery, swabs taken (normal)

What would you do next?

## Case study - Farzana

- Seen F2F in community gynaecology clinic
- Anterior labial fusion
- Pallor
- Inflammation of inner labia minora and loss of labia
- Clinical diagnosis of Lichen Sclerosus
- Topical estradiol continued but potent topical steroid prescribed to manage LS in line with BAD guidance



## Case study – Saira

- 57
- Started HRT 3 years ago under private menopause doctor
- PMH – migraine with aura
- BMI 24.3, non-smoker, occasional alcohol
- No relevant FHx
- Currently not taking HRT but intrusive sweats/flushes, marked anxiety affecting work, fatigue (all resolved with HRT)
- Really liked estradiol patches
- Every progestogen option has had side effects (micronized progesterone – rash (oral/PV), conti patches and MPA mood change/bloating/worsening fatigue)
- Not overly keen to try 52mg LNG-IUD

What else can you try??

# Options for progestogen intolerance

## Progestogen:

**Micronised Progesterone: Utrogestan 100mg** orally at night daily on continuous basis

Or **Provera a minimum of 2.5mg** orally daily on continuous basis

Or **Norethisterone 5mg** orally daily on continuous basis (1mg would be sufficient for use in a continuous combined regimen but not available in stand-alone preparations)

**Off license use of norethisterone in progestogen only contraceptive pills** (e.g. **Noriday** 3 x tablets of 350 micrograms a day, will provide 1.05mg of norethisterone) may be considered as an equivalent alternative.

Or **52mg Levonorgestrel IUD**

Or **Drospirenone 4 mg (Slynd)** 1 active hormonal tablet 4 mg can be taken daily on a continuous basis (omitting the 4 hormone free pills in the pack)

Off licence use of this progestogen-only contraceptive pill can be considered as an equivalent alternative for women experiencing progestogenic side effects with other preparations.

Earlier studies have reported that desogestrel 150 micrograms is effective as the progestogen component of HRT with no increase in the risk of endometrial hyperplasia. There is lack of evidence on the use of desogestrel 75 micrograms as the progestogen component of HRT.

If desogestrel 75 micrograms is used as contraception in women receiving HRT, it would be recommended to add further progestogen (e.g. Utrogestan 100 mg daily or 200 mg for 12 days a month) to provide adequate endometrial protection.

BRITISH MENOPAUSE SOCIETY Tool for clinicians

Information for GPs and other health professionals

1 of 8

The specialist  
authority for  
menopause & post  
reproductive health



## HRT preparations and equivalent alternatives

This document has been produced to provide healthcare professionals with information about equivalent HRT preparations.

<https://thebms.org.uk/wp-content/uploads/2024/02/15-BMS-TfC-HRT-preparations-and-equivalent-alternatives-JAN2024-B.pdf>

## Off label use:

- Noriday 3x 350mcg daily (but with previous HRT may not tolerate)
- 2xDesogestrel daily (150mcg daily) – again will she tolerate
- Slynd – 4mg Drospirenone daily (omit the green placebo pills each packet)



## Case study – Saira

What did I do:

Trial of Slynd 4mg daily alongside estradiol 50mcg patch twice weekly (initially half a patch twice weekly for first 4 weeks)

Review at 3 months:

- Mood dip (like PMS) in the first 6-8 weeks
- Spotting in the first 2-3 weeks after restarting, now no bleeding
- Feels well, mood improved, vasomotor symptoms resolved



## Case study – Hannah

- 52, attended for review in September 2023
- Stable on HRT for >12 months (Sandrena 1mg plus 100mg micronized progesterone daily), amenorrhoea
- PMH – asthma
- DH – inhalers, NKDA
- BMI 44, BP 126/82, non-smoker, alcohol 6 units/week
- Review September 2024
- Symptoms well controlled, no concerns, BMI now 27



## Case study – Hannah

- Any bleeding?

‘Not really ..... well only 6 months ago but that was just because I was using Mounjaro and all the forums told me this was normal’

- Referred for urgent pelvic ultrasound in line with BMS guidance

Anteverted uterus with endometrial thickening measuring up to 17mm, urgent gynaecology referral is advised

- Referred via USCP – hysteroscopy and biopsy – endometrial cancer stage 1A
- Underwent total hysterectomy and bilateral salpingo-oophorectomy
- Patient decided to wean HRT – currently using Paroxetine to manage VMS

## Use of incretin-based therapies in women using hormone replacement therapy (HRT)

### Introduction

Incretin-based therapies refers to a class of medications used for the treatment of diabetes and obesity that mimic the action of incretins — “gut hormones” that regulate insulin secretion, appetite and satiety, amongst other functions.

This BMS Tool for Clinicians will clarify:

- Background information about obesity and diabetes, the primary disease indications for incretin-based therapies
- Indications for the use of incretin-based therapies
- Considerations when prescribing incretin-based therapies in women using HRT during the menopause transition and post-menopause
- General guidance

This Tool for Clinicians will not cover all the effects of incretin-based therapies or their potential effects if used outside regulator approved indications.

### Background

Rates of obesity have more than trebled in the UK over the last 30 years in line with the worldwide obesity epidemic<sup>1</sup>. Complex environmental factors contribute to this increase and the World Health Organisation has shifted the focus from individual to societal causes.

According to NHS digital data from 2022, the proportion of overweight and obesity combined among women aged 45 to 54 was 64% with the rate of obesity being 34%. Rates among women aged 55 to 64 were 60% and 35% respectively.

A pragmatic approach to adjusting progesterone dosing with different HRT preparations, based on limited available evidence, is summarised in box below:

Current progestogen	Recommendation
Combined patch	No change
LNG-IUD up to 5 years	No change
Oral progestogen/progesterone*	Consider changing to LNG-IUD/increase dose of progestogen/progesterone at initiation for 4 weeks and maintain higher dose for 4 weeks after any dose increment
Vaginal progesterone (off licence)	No change

\* Weight loss injections may reduce the effectiveness of oral HRT medications. Review of current HRT is recommended while using these medications.

<https://thebms.org.uk/wp-content/uploads/2025/05/23-BMS-TfC-Use-of-incretin-based-therapies-APRIL2025-E.pdf>



## New products

1) Dydrogesterone 10mg tablets (Nalvee) - 2026

Sequential therapy - 10 mg dydrogesterone during the last 14 days of each 28-day cycle

Depending on the clinical response, the dosage may be adjusted to 20 mg daily

N.B. Product is not licensed as part of continuous combined HRT but equivalent dose in existing combined preparations is 2.5-5mg daily

2) Estradot Conti – two doses 30/95 and 40/130 (estradiol +norethisterone)

3) Fezolinetant/Elinzanetant - once NICE approval complete -?? 2026

- Fezolinetant (Veoza) 45mg once daily

- Elinzanetant (Lynkuet) 120mg once daily



Any questions?

THANK YOU

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