GYNAECOLOGY – Management of Menopause

University Hospitals of Leicester NHS
NHS Trust

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Contents

1. Introduction and Who Guideline applies to

This guideline is intended for the use of clinicians who are involved in providing service to the women presenting with menopausal symptoms referred to secondary care. This guideline covers women, trans men and non-binary people registered female at birth, who currently have menopause-associated symptoms or who will experience menopause in the future. The aim of this guideline is to fulfil the criteria of best service and best clinical practice which is evidence based and according to National Institute for Heath and Care Excellence.
(NICE https://www.nice.org.uk/guidance/ng23/menopause-identification-and-management)

Background:

According to the Office of National Statistics censes, there were around 7.25 million women between the age of 45 and 60 years in the UK in 2019. A consequence of increasing life expectancy has been an increase in the proportion of the UK population expected to survive to older ages which means the number of postmenopausal women is also increasing. This has resulted in more women seeking advice from GPs for the management of menopausal symptoms and more women are referred to secondary care for advice on control of symptoms and management of those who have associated long-term health issues.

Related Documents:
• Testosterone Replacement Therapy for Female Androgen Deficiency Syndrome (FADS) UHL Gynaecology Guideline
• Management of Unscheduled Bleeding in Women on Hormone Replacement Therapy (HRT) UHL Gynaecology Guideline

2. Guideline Standards and Procedures

2.1 Initial consultation & clinical assessment:

A detailed clinical assessment should be done at initial visit for menopausal symptoms and co-morbidities.
At initial consultation, a detailed history of menopausal symptoms should be taken to establish woman's attitude towards menopause and her opinions for different management options. Aim of relevant history including gynaecological, medical and family history should be to exclude any suspected pathology and to determine the risk factors for future illness secondary to menopause and or its treatment.
Physical examination such as the measurement of Blood Pressure (BP) and Body Mass Index (BMI) is recommended. Breast and pelvic examination are not routinely required but should be carried out if pathology is suspected from initial assessment.

2.2 Laboratory tests:

Routine Follicle Stimulating Hormone (FSH) levels should not be requested in symptomatic women over 45y or those taking high dose hormonal treatments.

Do not routinely use laboratory tests to diagnose perimenopause and menopause:

1. Do not use laboratory tests to diagnose the following in otherwise healthy women aged over 45 years with menopausal symptoms:
    - Perimenopause based on vasomotor/climacteric symptoms and irregular periods
    - Menopause in women who have not had a period for at least 12 months and are not using hormonal contraception/treatments
    - Menopause based on climacteric symptoms in women without a uterus

2. Do not use the following laboratory and imaging tests to diagnose perimenopause or menopause in women aged over 45 years:
    - Anti-Mullerian hormone
    - Inhibin A
    - Inhibin B
    - Oestradiol
    - Antral follicle count
    - Ovarian volume

3. Hormonal treatments and diagnosis of menopause:
It is important to understand that it can be difficult to diagnose menopause in women who are taking hormonal treatments (high dose progestogens), for example for the treatment of heavy periods or endometriosis.

4. Contraception and Menopause:
Do not use FSH to diagnose menopause in women using combined Oestrogen and progestogens contraception or high dose progestogens for example injectable progestogens which can result in menopausal symptoms due to its hypoestrogenic effect.

5. Consider using a FSH test on day 1-4 if still having periods (not intermenstrual bleeding or breakthrough bleeding on hormone therapy). Elevated FSH is suggestive of perimenopause only:
    - In women aged 40 to 45 years with menopausal symptoms, including a change in their menstrual cycle
    - Diagnose premature ovarian insufficiency in women aged under 40 years if no other cause for amenorrhoea and elevated FSH levels >30IU/L on 2 blood samples taken 4-6 weeks apart if
        - no periods for >12 months with a uterus with or without symptoms of the menopause
        - infrequent periods with a uterus and menopausal symptoms
        - symptoms of the menopause following hysterectomy with conservation of the ovaries (FSH not required if both ovaries removed)

- Normal FSH should not be used to withhold HRT in women over 40y, suffering symptoms of the menopause. Risk / benefits of HRT should be discussed and individualised treatment offered. Alternatively consider/offer combined oral contraception with 20mcg EE containing pill up to age 50y, if contraception also required.

2.3 Symptom management advice:

Women should be given general advice about how they can best manage climacteric symptoms.
https://www.womens-health-concern.org/help-and-advice/factsheets/menopause/
Clinicians should provide information to menopausal women and their family members or carers (as appropriate) that includes:

- An individualised approach at all stages of diagnosis, investigation and management of menopause.
- An explanation of the stages of menopause including common symptoms and diagnosis.
- Lifestyle changes and interventions that could help general health and wellbeing.
- Benefits and risks of treatments for menopausal symptoms.
- Long-term health implications of menopause and treatment.
- Role of complementary therapies and unregulated preparations.
- About starting and stopping HRT.
- About review and referral.

Explain to women that as well as a change in their menstrual cycle, they may experience a variety of symptoms associated with menopause, including:

- vasomotor symptoms (for example, hot flushes and sweats)
- musculoskeletal symptoms (for example, joint and muscle pain)
- effects on mood (for example, low mood) and anxiety
- cognitive dysfunction and memory problems
- urogenital symptoms (for example, vaginal dryness)
- sexual difficulties (for example, low sexual desire)
- hair loss

2.4 Lifestyle changes advice:

Lifestyle changes should be recommended to all climacteric women: Balanced diet, exercise, smoking cessation and alcohol reduction improves quality of life for women suffering with menopausal symptoms.

- Explain to women that obese women have more frequent menopausal symptoms than normal or overweight women, but the associated menopausal symptoms differed depending on the menopausal stage.
- Recommendations should include healthy life-style advice as part of menopausal symptom management to help with reduction in obesity and its associated risks.

- Recommend women eat a Mediterranean style diet and to exercise for 150 minutes per week to optimise a healthier lifestyle.
- Explain to people experiencing menopause the importance of maintaining muscle mass and strength through physical activity
- It is recommended to encourage women to stop smoking and refer to the stop the smoking service. Risk of death due to smoking reduces to 50% one year after stopping the treatment.
- Inform the women that the risk of breast cancer is doubled for women who used combined hormone therapy for 5 years of more and take more than one drink of alcohol per day.

2.5 Contraception advice:

Appropriate contraceptive advice should be given to women. Women should be informed that although a natural decline in fertility occurs with age and spontaneous pregnancy is rare after 50 years of age, effective contraception is required until menopause to prevent an unintended pregnancy but can be safely stopped at 55y. See guidance from the faculty of Sexual & Reproductive Healthcare on contraception for women aged over 40 years.
FSRH Clinical Guideline: Contraception for Women Aged over 40 Years (August 2017, amended July 2023) - Faculty of Sexual and Reproductive Healthcare
FSRH Guideline Contraception for Women Aged Over 40 Years

Table 8: Recommendations regarding stopping contraception

Contraceptive method	Age 40–50 years	Age >50 years
Non-hormonal	Stop contraception after 2 years of amenorrhoea	Stop contraception after 1 year of amenorrhoea.
Combined hormonal contraception	Can be continued	Stop at age 50 and switch to a non-hormonal method or IMP/POP/LNG-IUS, then follow appropriate advice.
Progestogen-only injectable	Can be continued	Women ≥50 should be counselled regarding switching to alternative methods, then follow appropriate advice.
Progestogen-only implant (IMP) **Progestogen-only pill (POP)** **Levonorgestrel intrauterine system (LNG-IUS)**	Can be continued to age 50 and beyond	Stop at age 55 when natural loss of fertility can be assumed for most women. ▶ If a woman over 50 with amenorrhoea wishes to stop before age 55, FSH level can be checked. ▶ If FSH level is >30 IU/L the IMP/POP/LNG-IUS can be discontinued after 1 more year. ▶ If FSH level is in premenopausal range then method should be continued and FSH level checked again 1 year later.
		A 52mg LNG-IUS inserted ≥45 can remain *in situ* until age 55 if used for contraception or heavy menstrual bleeding.

FSH, follicle-stimulating hormone; IU, international unit.

2.6 Management options for people aged 40 or over with menopause symptoms:

Discuss the benefits and risks associated with each potential management option for menopause-associated symptoms. Greene Climacteric Scale can be used to assess climacteric symptoms and monitor response to treatment (appendix 1)

2.6.1 Hormone replacement therapy

Consider the benefits and risks to the person's age, individual circumstances and potential risk factors. When discussing HRT, talk about the benefits and risks associated with:

- combined versus oestrogen-only HRT, which of the 2 types of HRT the person would be offered, and why)
- transdermal versus oral HRT
- types of oestrogen and progestogen
- sequential [scHRT] versus continuous combined HRT [ccHRT]
- dose and duration

If a person chooses to take HRT:

- discuss the possible duration of treatment at the outset
- at every review, rediscuss the benefits and risks of continuing treatment
- explain that symptoms may return when HRT is stopped and discuss the option of restarting treatment if necessary.

Offer psychological support to people who are experiencing early menopause and are distressed by their diagnosis or its consequences. If needed, refer them to psychology services.

2.6.2 Cognitive behavioural therapy

When discussing CBT as a possible management option, explain what CBT is (including menopause-specific CBT) and talk about the available options, considering the person's preferences and needs, for example:

- face-to-face or remote sessions
- individual or group sessions
- self-help options

CBT is not available via UHL gynaecology services. Patients can self-refer to Vita Health website for extra help.
https://www.vitahealthgroup.co.uk/make-a-referral/

2.6.3 HRT alternatives

Most prescribable alternative therapies have been evaluated for their impact on vasomotor symptoms. Some of them also have an impact on mood and well-being. Refer to BRITISH MENOPAUSE SOCIETY Tool for clinicians for details.
https://thebms.org.uk/wp-content/uploads/2022/12/02-BMS-TfC-Prescribable-alternatives-to-HRT-NOV2022-A.pdf

2.6.4 Complementary therapies and unregulated preparations

Explain to people with menopause-associated symptoms that the efficacy and safety of unregulated hormone preparations are unknown. The safety, quality and purity of constituents in unregulated preparations may be unknown.
Though, there is some evidence that isoflavones or black cohosh may relieve vasomotor symptoms associated with menopause, there are multiple preparations available, and their safety is uncertain, different preparations may vary and interactions with other medicines have been reported.

Advise people with a personal history of, or at high risk of, breast cancer that, although there is some evidence that St John's wort may help relieve vasomotor symptoms associated with menopause, there is uncertainty about appropriate dosage, persistence of effect, variation in the nature and potency of preparations and potential serious interactions with other medicines (including tamoxifen, anticoagulants and anticonvulsants).

2.7 Managing menopause symptoms

2.7.1 Vasomotor symptoms

Offer HRT to people with vasomotor symptoms after discussing with them the short-term (up to 5 years) and longer-term benefits and risks. Offer a choice of preparation's as follows:

- Oestrogen and progestogen (ccHRT) should be offered to women with a uterus and those who underwent hysterectomy for advanced endometriosis.
- Oestrogen alone to women without a uterus
- For women with history of subtotal hysterectomy, there is no consensus of management but ideally a sequential combined HRT for 3 months should be trialled and if there is no withdrawal bleed, then oestrogen-based therapy should be continued. Otherwise, consider ccHRT if there are concerns for presence of endometrial tissue in the cervical stump or withdrawal bleeding on scHRT.

Consider menopause-specific cognitive behavioural therapy (CBT) as an option for vasomotor symptoms associated with menopause:

- in addition to HRT or
- for people for whom HRT is contraindicated or
- for those who prefer not to take HRT

(Please refer to section 2.6.2 for further details)

Do not routinely offer selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) or clonidine as first-line treatment for vasomotor symptoms alone.

2.7.2 Genitourinary symptoms associated with menopause

2.7.2.1 People with no history of breast cancer

Offer vaginal oestrogen and review regularly. When discussing the option of vaginal oestrogen, explain that serious adverse effects are very rare. Vaginal oestrogen is absorbed locally – a minimal amount is absorbed into the bloodstream (when compared with systemic HRT), but this is unlikely to have a significant effect throughout the body.

Vaginal oestrogen can be used on its own or in combination with non-hormonal moisturisers or lubricants. Consider vaginal prasterone for genitourinary symptoms if vaginal oestrogen, or non-hormonal moisturisers or lubricants have been ineffective or are not tolerated.

Consider ospemifene as an oral treatment for genitourinary symptoms, if the use of locally applied treatments is impractical, for example, because of disability.

2.7.2.2 People with a personal history of breast cancer

Offer non-hormonal moisturisers or lubricants to people with a personal history of breast cancer and genitourinary symptoms associated with menopause.
Consider vaginal oestrogen if symptoms continue despite trying non-hormonal treatments. Vaginal oestrogen may be used in combination with a non-hormonal moisturiser or a lubricant. [This is an off-label use of vaginal oestrogen]
For people currently having aromatase inhibitors as adjuvant treatment for breast cancer, work with a breast cancer specialist to identify treatment options for genitourinary symptoms that have continued despite trying non-hormonal treatments.

- For people with a personal history of oestrogen receptor negative breast cancer, recognise that any oestrogen systemically absorbed from taking vaginal oestrogen is unlikely to increase the risk of breast cancer recurrence, and so it is likely to be safe.
- For people with a personal history of oestrogen receptor positive breast cancer, recognise that:
    - it is unknown whether any oestrogen systemically absorbed from taking vaginal oestrogen could increase the risk of breast cancer recurrence and
    - adjuvants that block oestrogen receptors in cancer cells (for example, tamoxifen) would reduce any such potential impact.

Vaginal laser treatment- Do not offer vaginal laser treatment for genitourinary symptoms associated with menopause unless as part of RCT.

2.7.3 Depressive symptoms / Psychological symptoms

Women commonly report symptoms of anxiety, depression and sleep disturbances but the symptoms of anger, brain fog, crying spell, irritability, loss of confidence and self-esteem, loss of joy, mood swings, anxiety, panic attacks and poor motivation should not be dismissed as these have a very significant detrimental effect on quality of life, work and relationships. Consider HRT to alleviate depressive symptoms with onset around the same time as other symptoms associated with menopause.
Consider CBT as an option for people who have depressive in association with vasomotor symptoms:

- in addition to other management options or
- for people for whom other options are contraindicated or
- for those who prefer not to try other options

(Please refer to section 2.6.2 for further details)

2.7.4 Sleep

Consider menopause-specific CBT as an option for people who have sleep problems (such as night-time awakening) in association with vasomotor symptoms:

- in addition to other management options (including HRT) or
- for people for whom other options are contraindicated or
- for people who prefer not to try other options.

(Please refer to section 2.6.2 for further details)

2.7.5 Altered sexual function

Consider testosterone supplementation for people with low sexual desire associated with menopause if HRT alone is not effective.
https://thebms.org.uk/wp-content/uploads/2022/12/08-BMS-TfC-Testosterone-replacement-in-menopause-DEC2022-A.pdf

2.8 Long term benefits and risks of HRT:

Long-term benefits and risks of hormone replacement therapy should be discussed with the patient. When started early enough, the benefits of body-identical HRT are widely considered to reduce the risk of heart disease, new-onset Type 2 diabetes, stroke, dementia, osteoporosis, colorectal cancer, and all-cause mortality.

2.8.1 Breast cancer:

Offer menopausal women with history of, or at high risk of, breast cancer:

- Information on all available treatment options
- In people with previous breast cancer, first-line treatment is lifestyle changes and HRT alternatives.
- SSRIs - Paroxetine, Fluoxetine and Sertraline should not be offered to women with breast cancer who are taking Tamoxifen
- Referral to a healthcare professional with expertise in menopause management

Inform that the baseline risk of breast cancer for women around menopausal age varies from one woman to another according to the presence of underlying modifiable and non-modifiable risk factors. Inform that any increased in the risk of breast cancer is related to treatment duration and reduces after stopping HRT

- There is little or no increase in the risk of breast cancer mortality with oestrogen-only HRT. This has been challenged in the new MHRA guidance*
- Breast cancer risk increases with combined HRT and the increase:
    - rises with duration of use
    - is higher in people currently taking HRT than in those who have taken it in the past
    - declines after stopping HRT but persists at least 10 years after stopping use.
- There is a very small increase in risk of death from breast cancer with combined HRT.
- Breast cancer risk with sequential combined HRT is lower than with continuous combined HRT but higher than without HRT.
- There is insufficient evidence to establish whether the increase in risk of breast cancer is different with preparations containing micronised progesterone or dydrogesterone from what it is with preparations containing other progestogens.

Stop systemic HRT in people who are diagnosed with breast cancer in line with the recommendations on menopause symptoms in NICE's guideline on early and locally advanced breast cancer
For advice on the treatment of menopausal symptoms in women with breast cancer or at high risk of breast cancer, see recommendations on complications of local treatment and menopausal symptoms in the NICE guideline on early and locally advanced breast cancer and recommendations on risk reduction and treatment strategies in the NICE guideline on familial breast cancer.
Early and locally advanced breast cancer: diagnosis and management NICE guideline [NG101]
Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer Clinical guideline [CG164]
MHRA 2019 advice

- *All forms of systemic HRT are associated with a significant excess incidence of breast cancer, irrespective of the type of oestrogen or progestogen or route of delivery (oral or transdermal)*
- *There is little or no increase in risk with current or previous use of HRT for less than 1 year; however, there is an increased risk with HRT use for longer than 1 year*
- *Risk of breast cancer increases further with longer duration of HRT use*
- *Risk of breast cancer is lower after stopping HRT than it is during current use, but remains increased in ex-HRT users for more than 10 years compared with women who have never used HRT*
- *Risk of breast cancer is higher for combined oestrogen-progestogen HRT than oestrogen-only HRT*
- *For women who use HRT for similar durations, the total number of HRT-related breast cancers by age 69 years is similar whether HRT is started in her 40s or in her 50s*
- *The study found no evidence of an effect on breast cancer risk with use of low doses of oestrogen applied directly via the vagina to treat local symptoms*

In the UK about 1 in 16 women who never use HRT are diagnosed with breast cancer between the ages of 50 and 69 years. This is equal to 63 cases of breast cancer per 1000 women. Over the same period (ages 50–69 years), with 5 years of HRT use, the study estimated:

- *about 5 extra cases of breast cancer per 1000 women using oestrogen-only HRT*
- *about 14 extra cases of breast cancer per 1000 women using oestrogen combined with progestogen for part of each month (sequential HRT)*
- *about 20 extra cases of breast cancer per 1000 women using oestrogen combined with daily progestogen HRT (continuous HRT)*

These risks are for 5 years of HRT use. The numbers of extra cases of breast cancer above would approximately double if HRT was used for 10 years instead of 5.

2.8.2 Venous thromboembolism

Explain to women that:

- The risk of venous thromboembolism (VTE) is increased by oral HRT compared with baseline population risk
- The risk associated with transdermal HRT given at standard therapeutic doses is no greater than baseline population risk
- Consider transdermal rather than oral HRT for menopausal women who are at increased risk of VTE, including those with a BMI over 30 kg/m2
- Consider referring menopausal women at high risk of VTE (for example, those with a strong family history of VTE or a hereditary thrombophilia) to a haematologist for assessment before considering oral HRT.

2.8.3 Coronary heart disease

Cardiovascular disease is leading cause of morbidity and mortality in postmenopausal women. For people with a personal history of coronary heart disease or stroke, ensure that combined or oestrogen-only HRT is discussed with and offered, if appropriate, by a healthcare professional with expertise in menopause.

Ensure that menopausal women and healthcare professionals involved in their care understand that HRT:

- Does not increase cardiovascular disease risk when started in women aged under 60 years and does not affect the risk of dying from cardiovascular disease
- Can significantly reduce the risk of cardiovascular mortality, heart failure or myocardial infarction when commenced within 6 years of menopause
- Use of HRT commenced between 6-10y of LMP neither increases or decreases the risk of cardiovascular disease
- Be aware that the presence of cardiovascular risk factors is not a contraindication to HRT as long as they are optimally managed (hypertension, high cholesterol) preferably used transdermal oestrogen.
- The baseline risk of coronary heart disease for women menopausal age varies from one woman to another according to the presence of cardiovascular risk factors
- Coronary heart disease risk does not increase with oestrogen-only HRT
- HRT with Oestrogen and progestogen is associated with little or no increase in the risk of coronary heart disease
- HRT does not provide secondary prevention of cardiovascular disease and NICE advises not to offer HRT for primary or secondary prevention of cardiovascular disease

2.8.4 Type 2 diabetes

The risk of developing type 2 diabetes does not increase with HRT. Generally, no adverse effect on blood glucose control is reported when taking HRT. The risk is not affected whether HRT is taken orally or trans-dermally.

Consider HRT for menopause-associated symptoms in people with type 2 diabetes after taking comorbidities into account and seeking specialist advice if needed.

2.8.5 Osteoporosis:
The baseline population risk of fragility fracture is low in the UK for women, trans men and non-binary people registered female at birth who are around the age of menopause and varies from one person to another.
Fragility fracture risk is decreased while taking HRT, both combined and oestrogen only HRT and this benefit is maintained during treatment but decreases once treatment stops and may continue for longer in people who take HRT for longer.
Give women advice on bone health and discuss these issues at review appointments (see the NICE guideline on osteoporosis: assessing the risk of fragility fracture).

2.8.6 Loss of muscle mass and strength:
Explain to women that musculoskeletal pain is more common in perimenopausal and postmenopausal women. Though not all musculoskeletal pain is arthralgia or arthritis, women have increased prevalence of osteoarthritis and rheumatoid arthritis in this age group; hence prompt referral should be done.
Muscle mass and strength decreases with age and there is limited evidence suggesting that HRT may improve muscle mass and strength. Musculoskeletal aches and pains symptoms secondary to menopause with no underlying pathology may respond to HRT. Physical activity is essential in maintaining muscle mass and strength.

2.8.7 Dementia:
Dementia risk might increase with combined HRT if it is started at 65 or over.
Dementia risk is unlikely to increase with oestrogen-only HRT.
NICE advises not to offer HRT for the purpose of dementia prevention.

2.8.8 Endometrial Cancer:
Endometrial cancer risk decreases with continuous combined HRT. The risk may slightly increase with sequential combined HRT, and the increase may be greater with longer duration of use, fewer days of progestogen per cycle and increased dosage of oestrogen.
In people with a uterus, endometrial cancer risk increases with oestrogen-only HRT, both oral and transdermal.

2.8.9 Ovarian Cancer:
The baseline population risk of ovarian cancer in women aged under 60 is very low.
In people with ovaries, there is a very slight increase in ovarian cancer risk with combined HRT. The risk increases very slightly after 5 years of using oestrogen-only HRT and this risk increases with duration of use.

2.8.10 Stroke:
The baseline population risk of stroke in women aged under 60 is very low.

- Stroke risk is unlikely to increase with the use of combined HRT or Oestrogen only HRT that includes transdermal oestrogen.
- Stroke risk increases with combined HRT containing oral oestrogen and the increase:

    - rises with higher oestrogen dosage and longer duration of treatment, for example, if used for more than 5 years
    - is greater with increasing age at first starting HRT
    - differs between ethnic groups and may be greater in Black people.
- Stroke risk increases with oral oestrogen only HRT and the increase:
    - rises with the dosage of oestrogen
    - is greater if HRT is started after the age of 60.

2.8.11 Planned medical or surgical treatment that is likely to result in menopause:
Offer people who are likely to experience menopause as a result of medical or surgical treatment the opportunity to discuss fertility, both before and after they have their treatment, with a healthcare professional with expertise in fertility.
Offer people who are likely to experience menopause as a result of medical or surgical treatment the opportunity to discuss menopause, both before and after they have their treatment, with a healthcare professional with expertise in menopause.

2.8.12 Gender-affirming hormone therapy: past use
Ensure that trans men or non-binary people registered female at birth who have taken gender-affirming hormone therapy in the past and have symptoms associated with menopause can discuss these with a healthcare professional with expertise in menopause.
Consider menopause-specific CBT for vasomotor symptoms, difficulties with sleep or depressive symptoms associated with menopause for trans men and non-binary people registered female at birth who have taken gender-affirming hormone therapy in the past. CBT could be used:

- in addition to other management options or
- for people for whom other options are contraindicated or
- for those who prefer not to try other options

(Please refer to section 2.6.2 for further details)

2.8.13 All-cause mortality (life expectancy)
Overall, life expectancy is unlikely to change with the use of combined HRT or oestrogen-only HRT.

2.8.14 Bleeding on HRT:
Women should be given advice on what to do in the event of bleeding whilst on HRT. Explain to women with a uterus that unscheduled vaginal bleeding is a common side effect of HRT within the first 6 months of treatment. If unscheduled bleeding continues in low-risk women, after six months of adjustments, discuss the options of an urgent ultrasound (within six weeks) versus weaning off HRT and consideration of non-hormonal alternatives (to avoid invasive investigations).
(Follow Management of Unscheduled Bleeding in Women on Hormone Replacement Therapy (HRT) UHL Gynaecology Guideline or National guidance)

2.9 Diagnosing and managing premature ovarian insufficiency:

Diagnosis and initial management or premature ovarian insufficiency should be undertaken by a clinician with appropriate experience of the condition.

2.9.1 Diagnosing premature ovarian insufficiency (POI):

Take into account the woman's clinical history (for example, previous medical or surgical treatment) and family history when diagnosing premature ovarian insufficiency.

- Primary causes of POI include chromosomal and genetic abnormalities, enzyme deficiencies and autoimmune diseases
- Secondary causes would be due to radiotherapy, chemotherapy, bilateral oophorectomy, hysterectomy without oophorectomy, uterine artery embolization and infections.

Diagnose premature ovarian insufficiency in women aged under 40 years based on:

- Menopausal symptoms, including no or infrequent periods (taking into account whether the woman has a uterus) **and** elevated FSH levels >30 IU/L on 2 blood samples taken 4-6 weeks apart
- Do not diagnose premature ovarian insufficiency on the basis of a single blood test
- Do not routinely use anti-mullerian hormone testing to diagnose premature ovarian insufficiency
- Offer women the tests including Thyroid Function test (TFT), Bone Mineral density (BMD) assessment, autoantibody screen to diagnose cause of POI.
- Perform Karyotyping for chromosomal abnormalities for POI under 30 years of age.
- Perform investigations for secondary diseases where indicated, for example, Diabetes, Addison's disease.

2.9.2 Managing premature ovarian insufficiency:

Explain to women with premature ovarian insufficiency:

- The importance of starting hormonal treatment either with HRT of a combined hormonal contraceptive and continuing treatment until at least the age of natural menopause (unless contraindicated)
- That the baseline population risk of diseases such as breast cancer and cardiovascular disease increases with age and is very low in women aged under 40
- That HRT may have a beneficial effect on blood pressure when compared with a combined oral contraceptive
- That both HRT and combined oral contraceptives offer bone protection
- That HRT is not a contraceptive
- If there are contraindications to hormonal treatments, provide information on bone and cardiovascular health, and symptom management

Consider referring women with premature ovarian insufficiency to healthcare professionals who have the relevant experience to help them manage all aspects of physical and psychosocial health related to their condition.

2.10 Starting HRT:
For people who wish to take hormone replacement therapy (HRT) for symptoms associated with menopause:

- offer combined HRT to people with a uterus, those who underwent hysterectomy for advanced endometriosis and with history of subtotal hysterectomy and concerns for presence of endometrial tissue in the cervical stump.
- offer oestrogen-only HRT to people who have had a total hysterectomy.

For people with a condition that may be affected by HRT, consider seeking advice on the choice of HRT from a healthcare professional with specialist knowledge of that condition.
If a person chooses to take HRT, use the lowest effective dosage.
Explain to people with a uterus that vaginal bleeding is a common side effect of systemic HRT within the first 3 months of treatment, and they will be asked about this during their 3-month review. Advise them to seek medical help promptly if they experience vaginal bleeding after 3 months.

2.11 Stopping HRT:
Offer women who are stopping HRT a choice of gradually reducing or immediately stopping treatment.

- Gradually reducing HRT may limit recurrence of symptoms in the short term
- Gradually reducing or immediately stopping HRT makes no difference to their symptoms in the longer term.

Stop systemic HRT in people who are diagnosed with breast cancer in line with the recommendations on menopause symptoms in NICE's guideline on early and locally advanced breast cancer.

2.12 Follow-up:
Women should be reviewed after 3 months and thereafter annually. Patients can be discharged to the GP once stable on treatment for review annually by the GP. Referral should be made to the Complex Menopause Clinic where necessary.
Review each treatment for short-term menopausal symptoms:

- Re-discuss the benefits and risks of continuing each treatment option.
- At 3 months, to assess efficiency and tolerability and need for adjustments to HRT regime
- The GP will review HRT annually thereafter unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events).
- Discuss bone health and lifestyle modifications at each review.

Refer women to a healthcare professional with expertise in menopause (Complex Menopause Service)

- If treatments do not improve menopausal symptoms
- On-going troublesome side effects
- Contraindications to HRT
- Uncertainty about the most suitable treatment option.

Refer women to UHL Complex Menopause Clinic where appropriate:

- Patient with history of / at increased risk of breast cancer, past personal history of VTE and other contraindications
- Patient with or at risk of osteoporosis
- Menopausal symptoms not improved despite HRT from GPs/ gynaecological colleagues
- Uncertainty about most suitable option for menopausal symptoms including testosterone therapy
- With troublesome side effects
- Persistent unexplained unscheduled bleeding on HRT (after ruling out EH), unresponsive to manipulation in progesterone as per guideline on 'Management of Unscheduled Bleeding on HRT'
- Primary ovarian insufficiency

3. Education and Training

Teaching sessions on management of menopause an evidence-based approach for junior doctors

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Quality of life (QOL) assessment for women using estradiol implants at follow up visit	Audit	S Malik	Once	Audit meeting
Management of menopausal symptoms for women with breast cancer	Audit	S Malik	Once	Audit meeting
Short term symptom control for women diagnosed with Premature ovarian insufficiency (POI)	Audit	S Malik	Once	Audit meeting
Role of estradiol level assessments for women on HRT	Audit	S Malik	Once	Audit meeting

5. Supporting references

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10. BMS Management of unscheduled bleeding on HRT

6. Key Words

HRT- hormone replacement therapy
FSH- Follicle stimulating hormone
SSRIs- selective serotonin reuptake inhibitors
SNRIs- serotonin and norepinephrine reuptake inhibitors
POI- premature ovarian insufficiency

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

EDI Statement

We are fully committed to being an inclusive employer and oppose all forms of unlawful or unfair discrimination, bullying, harassment and victimisation.

It is our legal and moral duty to provide equity in employment and service delivery to all and to prevent and act upon any forms of discrimination to all people of protected characteristic: Age, Disability (physical, mental and long-term health conditions), Sex, Gender reassignment, Marriage and Civil Partnership, Sexual orientation,

Pregnancy and Maternity, Race (including nationality, ethnicity and colour), Religion or Belief, and beyond.

We are also committed to the principles in respect of social deprivation and health inequalities.

Our aim is to create an environment where all staff are able to contribute, develop and progress based on their ability, competence and performance. We recognise that some staff may require specific initiatives and/or assistance to progress and develop within the organisation.

We are also committed to delivering services that ensure our patients are cared for, comfortable and as far as possible meet their individual needs.

CONTACT AND REVIEW DETAILS			
Guideline Lead (Name and Title) Samina Malik Consultant Mathews Anju			**Executive Lead** Chief medical officer
Details of Changes made during review:			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
March 2025		Mathews Anju	Changes • Cognitive behavioural therapy to manage symptoms associated with the menopause • managing genitourinary symptoms associated with the menopause • the effects of hormone replacement therapy (HRT) on specific health outcomes. Changes have been made to the wording to bring the language and style up to date.

Appendix 1: Risks & Benefits of HRT

Table 1: NICE data

Risks and Benefits of HRT for 1000 women aged 50-59y using HRT for 7.5 years (95% CI)[1]based on RCT (NICE Data)					
Conditions	Baseline population risk	Estrogen alone		Estrogen + Progestogen	
		Current user	>5 years since stopping treatment	Current user	>5 years since stopping treatment
Cardiovascular	26.3	6 fewer	6 fewer	5 more	4 more
Stroke	11.3	0	1 more	6 more	4 more
Breast cancer	24.4	6 fewer	6 fewer	5 more	8 more

Table 2: BNF data

Risks and Benefits of HRT for 1000 women in Europe aged 50-59y using HRT (BNF data)						
Conditions	Baseline population risk		Estrogen alone		Estrogen + Progestogen	
	5 years duration	10 years duration	5 years duration	10 years duration	5 years duration	10 years duration
Endometrial cancer	2	4	4 more	32 more	NS	NS
Ovarian cancer	2	4	<1 more	1more	<1 more	1more
Venous Thromboembolism	5	-	2 more	-	7more	-

NS(not significant difference)

Appendix 2: HRT Preparations

1-Vaginal estrogen

For genitourinary syndrome of menopause (GSM)

Brand	Type	Maintenance regimen	Type of Estrogen	Cautions	Prescription needed	Estrogen per dose	Estrogen per week
Vagifem, Vagirux	Vaginal tablet	2x per week	Estradiol		✓	10mcg	20mcg
Gina	Vaginal tablet	2x per week	Estradiol		✗	10mcg	20mcg
Estring	Silicon ring	Every 3 months	Estradiol		✓	7.5mcg/24h	52.5mcg
Imvaggis	Vaginal pessary	2x per week	Estriol		✓	30mcg	60mcg
Blissel	Vaginal gel	2x per week	Estriol	Contains parabens	✓	50mcg	100mcg
Ovestin	Vaginal cream	2x per week	Estriol	Care with peanut allergy as contain arachis oil	✓	500mcg	1000mcg

2-Sequential Combined HRT: Contains daily Estrogen and cylical progestogen/Progesterone

For perimenopausal women only

Type	Name	Estrogen	Progesterone	Dose
Patch	Evorel Sequi	Estradiol hemihydrate 50mcg/day	Norethisterone acetate 170mcg/day for 14/7	Twice weekly
	Femseven sequi	Estradiol hemihydrate 50mcg/day	Levonorgestrel 10 mcg/day for 14/7	Once weekly
Oral	Elleste Duet 1mg/2mg	Estradiol hemihydrate 1/2mg	Norethisterone acetate 1mg (12/7)	Daily
	Novofem	Estradiol hemihydrate1mg	Norethisterone acetate1mg (12/7)	Daily
	Femoston 1/10 Femoston 2/10	Estradiol hemihydrate 1/2mg	Dydrogesterone 10mg (14 /7)	Daily
	Trisequens	Estradiol hemihydrate1-2mg	Northisterone acetate 1mg (10/7)	Daily

3-Continuous Combined HRT: Contains daily Estrogen and progestogen/Progesterone

1- For postmenopausal women (>12m since LMP)
2- Swap from sequential combined to continuous combined:
   - after >5 years
   - or age of 54 years and over

Type	Name	Estrogen	Progesterone	
Patch Use patches preferentially if >60y, overweight or has migraines	Evorel Conti	Estradiol hemihydrate 50mcg/24h	Norethisterone acetate 170mcg per 24h (2 patches/w)	
	Femseven Conti	Estradiol hemihydrate 50mcg/24h	Levonorgestrel 7mcg per 24h (1 patch/w)	
Oral	Premique Low Dose	Conjugated equine estrogen 300mcg	Medroxyprogesterone acetate 1.5mg	
	EllesteDuet Conti	Estrodiol hemihydrate 2mg	Norethisterone acetate 1mg	
	Kliovance	Estradiol hemihydrate 1mg	Norethisterone acetate 0.5mg	
	Kliofem	Estradiol hemihydrate 2mg	Norethisterone acetate 1mg	
	Indivina 1/2.5, 1 /5, 2 /5	Estradiol valerate 1/2mg	Medroxyprogesterone acetate 2.5/5.0mg	Contains gelatin
	Femoston Conti	Estradiol hemihydrate0.5/1mg	Dydrogesterone2.5/5.0mg	
	Bijuve	Estradiol hemihydrate 1mg	Micronised progesterone 100mg	Contains gelatin

4-Estrogen-only (only if no uterus/Mirena in place)

Transdermal: may have fewer VTE/CVA risks so use preferentially if >60y, overweight or has migraines

Route	Name	Estrogen	Dose
Patch	Evorel 25/50/75/100	Estradiol hemihydrate 25/50/75/100mcg per 24h	Twice weekly
	Estraderm MX 25/50/75/100	Estradiol hemihydrate 25/50/75/100mcg per 24h	Twice weekly
	Estradot 25/37.5/50/75/100	Estradiol hemihydrate 25/37.5/50/75/100mcg / day	Twice weekly
	Femseven 50/75/100	Estradiol hemihydrate 50/75/100mcg per 24h	Weekly
	ProgynovaTS 50/100	Estradiol hemihydrate 50/100mcg per 24h	Weekly
Gel	Oestrogel Pump-Pack	Estradiol gel (0.06%) 1–4	1-4 pumps daily

	750 micrograms/actuation Gel 80g pump	pumps (0.75–3.0mg) per 24h	
	Sandrena 0.5/1.0mg sachets	Estradiol hemihydrate gel (0.1%) 0.5–1.5mg per 24h	One sachet daily
Spray	Lenzetto 8.1ml (56 actuations)	Estradiol hemihydrate 1.53mg/metred dose 1-3 sprays per 24h	1-3 sprays daily
Oral	Zumenon 1/2	estradiol hemihydrate1/2mg	daily
	Elleste Solo 1/2	Oestradiol hemihydrate 1/2mg	daily
	Progynova 1/2	Oestradiol valerate 1/2mg	daily
	Premarin 0.3mg 0.625mg 1.25mg	Conjugated equine estrogen 300mcg/625mcg/1.25mg	Daily Equine

5-Progestogen/progesterone-only (with estrogen-only HRT if has uterus)

Route	Progestogen	Dose	Name
Oral	Medroxyprogesterone acetate	10mg daily for 14d/cycle (sequential) or 5mg continuously (continuous combined)	Provera 2.5/5/10
Oral/ vaginal	Micronised progesterone (can be used vaginally: off-licence)	200mg for 10–12d/cycle (sequential) or 100mg daily (continuous combined)	Utrogestan
Intra-uterine	Levonorgestrel IUD 52mcg	20mcg/24h	Mirena, Benilexa

6-Other HRT Preparations

Route	Content	Dose	Name
Oral	Tibolone (gonadomimetic)	2.5mg once daily	Livial
	COC	Estradiol hemihydrate 1.5mg 2.5 mg nomegestrol	Zoely not yet on LMSG so GPs can't prescribe
	COC with variable dose of estrogen and progestogen	Estradiol valerate 1-3mg Dienogest 2-3mg	Qlaira not yet on LMSG so GPs can't prescribe
Vaginal	DHEA	6.5mg once daily bedtime	Intrarosa – Yellow on LMSG
Oral for vaginal atrophy	Ospemifene	60mg once daily	Senshio not yet on LMSG so GPs can't prescribe

Licensed estrogen dose and proportionate progestogen dose

BMS has recommended that 'The dose of the progestogen should be proportionate to the dose of estrogen. Women who require high dose estrogen intake should consider having their progestogen dose increased to ensure adequate endometrial protection.'
As part of an individualised menopause care, it is essential to tailor it according to menopause symptoms, bleeding pattern, background risk factors for breast and endometrial cancer. If needed serum assessment of estradiol levels to use as a guide.

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

Estrogen	Ultra-low dose	Low dose	Standard dose	Moderate dose	High dose
Oestrogel	½ pump	1 pump	2 pumps	3 pumps	4 pumps
Sandrena (gel)	0.25 mg (½sachet)	0.5 mg	1 mg	2 mg	3* mg
Lenzetto (spray)	1 spray	2 sprays	3 sprays	4-5 sprays	6* sprays
Patch	12.5 ug (½ patch)	25-37.5 µg	50 µg	75 µg	100 µg
Oral tablets	0.5 mg	1 mg	2 mg	3 mg	4 mg

* *Off-license use – rarely required to achieve symptom control*

Progestogen dose per licensed estrogen dose in the baseline population

Estrogen dose	Micronised progesterone		Medroxy progesterone		Norethisterone	
	Sequential	Continuous	Sequential	Continuous	Sequential	Continuous
Ultra/ Low	200 mg	100 mg	10 mg	2.5 mg	5* mg	5* mg
Standard	200 mg	100 mg	10 mg	2.5-5 mg	5* mg	5* mg
Moderate	200 mg	100 mg	10 mg	5mg	5 mg	5 mg
High	300 mg^{+}	200mg^{+}	20^ mg	10^ mg	5 mg	5 mg

LNG-IUS is for 5 years.

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

^ There is limited evidence in relation to optimal **MPA** dose with high dose estrogen; the advised dose of 10 mg providing protection with up to moderate dose estrogen.

+ There is limited evidence in relation to **optimal micronised progesterone** dose for moderate or high dose estrogen; the advised dose is based on studies reporting 100 mg/day providing protection with up to standard dose estrogen. If unscheduled bleeding occurs with ultra-low to moderate dose estrogen, and other progestogens are not acceptable, offer micronised progesterone at the dosage recommended for high dose estrogen.

Appendix 3:Suitable HRT for vegans and vegetarians

For Vegans

Estrogen only

- Gel- Oestrogel, Sandrena
- Patch – Estradot, Evorel, Progynova TS, Estraderm MX
- Spray – Lenzetto

Progesterone and Progestogens

- Cyclogest, Crinone – unlicensed for HRT
- Mirena – device does not contain any animal product but the inserter has and is thrown away after use hence might not be suitable for vegans.
- Levosert, Benilexa – not licensed for HRT but can be used for this purpose as per BMS advice

Combined HRT (E+P)

- Patch – Evorel conti, Evorel Sequi, Femseven conti, Femseven Sequi

Vaginal Estrogen

- Ovestin cream, blissel gel, Imvaggis pessary, Estring

Testosterone

- Testogel, Testim, Tostran, Androfeme

Additional options for vegetarians

Estrogen only – Elleste Solo, Zumenon, Progynova

Progesterone and Progestogens only

- Lutigest pessary- not licensed for HRT, contain lactose
- Provera, Noethisterone

Combined HRT (E+P)

- Femoston, Femoston conti, Elleste Duet Conti, Kilofem, Tibolone

Vaginal Estrogen - Vagifem, Vagirux

Appendix 4: Greene Climacteric scale

Greene Climacteric Scale

The Greene Scale provides a brief measure of menopause symptoms. It can be used to assess changes in different symptoms, before and after menopause treatment. Three main areas are measured:
1. Psychological (items 1-11). 2. Physical (items 12-18). 3. Vasomotor (items 19, 20).

Please indicate the extent to which you are bothered at the moment by any of these symptoms by placing a tick in the appropriate box:

SYMPTOMS	Not at all 0	A little 1	Quite a bit 2	Extremely 3	
1. Heart beating quickly or strongly					
2. Feeling tense or nervous					
3. Difficulty in sleeping					
4. Excitable					
5. Attacks of anxiety, panic					
6. Difficulty in concentrating					
7. Feeling tired or lacking in energy					
8. Loss of interest in most things					
9. Feeling unhappy or depressed					
10. Crying spells					
11. Irritability					
12. Feeling dizzy or faint					
13. Pressure or tightness in head					
14. Parts of body feel numb					
15. Headaches					
16. Muscle and joint pains					
17. Loss of feeling in hands or feet					
18. Breathing difficulties					
19. Hot flushes					
20. Sweating at night					
21. Loss of interest in sex					
Score					Total

Greene, J, *A factor analytic study of climacteric symptoms* **Journal of Psychosomatic Research** (1976), 20, 425—430.