Managing common problems in the menopause

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The menopause is a normal life event for women and not an illness or medical condition. Despite this, menopause can predispose vulnerable women to distressing symptoms that impact adversely on their quality of life and to long term medical conditions such as osteoporosis, cardiovascular disease and dementia. Many healthcare professionals are uncertain about the management of the menopause, and this leads to many women not receiving treatment which is often beneficial to them. This article will cover the diagnosis of the menopause including premature ovarian insufficiency. Some of the health risks of the menopause will be discussed and treatment of the menopause, with a particular focus on hormone replacement therapy, will be covered in detail.

The GP curriculum and the menopause

Clinical module 3.06: Women’s health requires GPs to:
- Recognise and manage common medical conditions encountered in generalist medical care. It includes safe prescribing and medicines management approaches
- Demonstrate an understanding of the importance of risk factors in the diagnosis and management of women’s problems
- Know how the social and biological features of the perimenopause and menopause period interact and affect heath, social well-being and relationships (e.g. mood swings, anxiety and depression, reduced libido)
- Be able to advise on prevention strategies relevant to women (e.g. osteoporosis)

Background

The menopause occurs a year after a woman’s last menstrual period. Symptoms of the menopause can occur before this time, during the perimenopause, and also after this time, when a woman is postmenopausal (Box 1).

In the early-1900s the average age of the menopause was 57 years, and a woman’s life expectancy was around 59 years. However, the average age of the menopause is now 51 years and a woman’s life expectancy is around 82 years. This means that many women are postmenopausal for around 30 years or more, which can have a negative impact on the quality of their lives.
Many women are affected by symptoms of their menopause, often to the detriment of their families, work and life in general. In addition, many women do not realise that there are health risks to having low oestrogen levels in their bodies; these include increased risk of cardiovascular disease and osteoporosis. The predisposition to cardiovascular disease is due to an adverse effect on lipids, lipoproteins, insulin resistance and arterial compliance. Loss of bone density, and ultimately osteoporosis, occurs due to an increase in bone breakdown by osteoclastic activity which exceeds bone formation by osteoblasts.

Guidelines on the menopause were published in November 2015 by The National Institute for Health and Care Excellence (NICE) and menopause care in the UK should be based on these guidelines (NICE, 2015a). These are the first clinical guidelines on menopause to be produced by NICE and provide clear recommendations on both the diagnosis and treatment of women with menopausal symptoms.

### Symptoms of the menopause

The majority of women experience symptoms of the menopause; however, they vary between women and often fluctuate during the months. Many women do not even recognise some of their symptoms as being related to the perimenopause and menopause. The psychological symptoms of the menopause are the ones that usually affect women the most, and are often misdiagnosed as depression.

There are many symptoms that can occur and they usually vary between different women. The more common symptoms are listed in Box 2.

### Urogenital atrophy

The term vulvovaginal atrophy (VVA) (or atrophic vaginitis) is often used to describe symptoms that can arise due to vaginal dryness, but it does not include the urinary symptoms that frequently occur in people with VVA. The term genitourinary syndrome of the menopause (GSM) is increasingly used, as this includes the urinary symptoms which often also occur (Portman et al., 2014).

Vaginal dryness and GSM are extremely common, with some studies showing prevalence figures as high as 80% in postmenopausal women (Palma et al., 2016). However, this condition is under recognized, as it is often not talked about during consultations; the majority of women do not voluntarily disclose their symptoms to their healthcare professional (Cagnacci et al., 2016). It is really important, therefore, to ask the right questions in order to make the diagnosis and then be able to offer the correct treatment (Box 3).

### Box 1. Definitions.

- **Perimenopause**: This is also sometimes called the menopause transition and it is the interval in which many women have irregular menstrual cycles before the menopause up to a year after her last period
- **Menopause**: This refers specifically to a year after a woman’s last menstrual period (LMP) so this is a retrospective diagnosis
- **Postmenopause**: This starts a year after LMP (so after the menopause)

### Box 2. Common symptoms of the menopause.

- **Vasomotor symptoms**
  - These are hot flushes and night sweats
  - Occur in around 75% of postmenopausal women, with 25% of these being severely affected
  - Mechanism is possibly due to the narrowing of the thermoregulatory-neutral zone, associated with over-reaction to changes in temperature
- **Other symptoms may include**:
  - Musculoskeletal symptoms (joint and muscle pains)
  - Effects on mood (low mood, irritability, anxiety and mood swings)
  - Urogenital symptoms (vaginal dryness, itching, increased frequency of micturition)
  - Sexual difficulties (loss of libido, dyspareunia)
  - Worsening frequency and severity of migraines
  - Poor concentration and reduced memory
  - ‘Brain fog’

Note: Symptoms of the menopause often last far longer than most women anticipate. Symptoms may resolve in 2-5 years, but they often last 10 years or longer.

### Box 3. Suggested questions to ask regarding making a diagnosis of GSM.

- Have you noticed any vaginal dryness or less vaginal discharge?
- Have you experienced any vaginal soreness, irritation or burning?
- Do you have any itching around your vagina or vulval area?
- Is sexual intercourse painful or uncomfortable?
- Have you noticed any urinary symptoms such as passing urine more often or being less able to hold on to your urine?
- Do you have any discomfort on passing urine?
As there are oestrogen receptors present in the vagina, urethra, bladder trigone, and pelvic floor, a lack of oestrogen can affect all these areas. The most common symptom of GSM is usually vaginal dryness, which can lead to dyspareunia. However, GSM is very common in women who are not sexually active, so it is important to also ask these women about these symptoms. Other symptoms can include vaginal irritation and itching, which can interfere with sleep, general enjoyment of life, and mood. Many patients have discomfort exercising, walking or even sitting down. Although many other menopausal symptoms improve with time, symptoms of GSM often worsen with age.

The vaginal mucosa can become drier, thinner, less elastic, and more fragile. There is often a decline in vaginal secretions and a decreased production of glycogen from the vaginal epithelium, which when associated with an increase in vaginal pH can increase the risk of local infections such as bacterial vaginosis and thrush (MacBride et al., 2016).

Making a diagnosis of menopause

The diagnosis of the perimenopause and menopause is usually a clinical diagnosis. NICE are very clear regarding making a diagnosis of the menopause (NICE, 2015a) and their recommendations are listed in Box 4.

Box 4. NICE recommendations regarding diagnosis of the menopause.

- Blood tests are not necessary in women with menopausal symptoms who are aged over 45 years and are otherwise healthy
  - Diagnosis of perimenopause is based on vasomotor symptoms and irregular or changing periods
  - Diagnosis of menopause can be made in women who have not had a period for at least 12 months and are not using hormonal contraception
  - Diagnosis of menopause can be based on symptoms in women without a uterus
- This means that for women over 45 years with menopausal symptoms or presenting with amenorrhea over 12 months, investigations are now no longer necessary to diagnose their menopause.
- In those women aged under-45 years: FSH may sometimes be used to diagnose the menopause
- A FSH level can be considered in the following women:
  - Those women aged 40-45 years with menopausal symptoms, including a change in their menstrual cycle
  - Those women aged under 40 years in whom menopause is suspected (See POI section)

Source: NICE, 2015a.

Follicle-stimulating hormone (FSH) measurements in the perimenopause in women over 45 years in age are not precise, as they fluctuate considerably over short periods of time. This means that they can be falsely reassuring.

Approximately 70% of FSH tests are currently performed in women over the age of 45 years, which is no longer appropriate. Reducing the number of FSH blood tests has the potential to bring significant cost savings to the NHS; it has been estimated that reducing unnecessary FSH testing could lead to a national saving of £9,600,000 (NICE, 2015b).

A FSH test may be useful in women below the age of 45 years to confirm the diagnosis of menopause; it can also be instructive regarding the ongoing requirement for contraception. This is particularly helpful in women on progestogen-only contraception, for example, levonorgestrel intrauterine system, who may not be having periods. Women on combined hormonal contraception should be advised to stop treatment for at least 6 weeks before having a FSH level taken (FSRH, 2017).

Other tests are largely unnecessary. This means that in practice women can start treatment sooner, which will be advantageous for many women, especially those with more severe symptoms.

Individualised care

When discussing menopause with women, it is very important that they receive individualised care, so their individual risks are discussed in the consultations. Women should receive appropriate information, ideally written, which will enable them to make informed choices regarding the treatment they receive. Receiving this information will help to enable them to make informed choices regarding the treatment they receive. They should also be signposted to accurate and appropriate websites.

This information should include:
- An explanation of the stages of menopause
- Common symptoms and diagnosis
- Lifestyle changes and interventions
- Benefit and risks of the range of treatments for menopausal symptoms
- Long-term implications of menopause

This individualised approach should be undertaken at all stages of diagnosis, investigation and management of menopause. Any treatment and care given to women should consider individual needs and preferences. When relevant, information about contraception should be given.

Management of the menopause

An informative consultation about the menopause should be seen as an ‘opportunity’. This is because correct medical intervention and advice at this point of life can offer women years of benefits from preventive healthcare.

Lifestyle recommendations regarding diet, exercise, smoking cessation and safe levels of alcohol consumption should be encouraged.
in all women. It is important to ensure that women are up to date with cervical and breast screening programmes, as appropriate. It is important that women are given clear information about the menopause and treatments, which is ideally in written form. A list of useful websites for patients (and also for healthcare professionals) is presented in Box 5.

**Box 5. Useful websites.**

- www.menopashedoctor.co.uk
- www.hormonehealth.co.uk
- www.thebms.org.uk
- www.daisynetwork.org.uk
- www.pcwhf.co.uk
- www.nice.org.uk
- www.menopausematters.co.uk
- www.pms.org.uk

Hormone replacement therapy (HRT) is only one part of the management of perimenopausal and menopausal women. For women who cannot take HRT or do not want to take HRT then there is some evidence that medication such as selective serotonin receptor inhibitors and selective noradrenaline receptor inhibitors can be beneficial (NICE, 2015a). However, these should not be offered as first line treatment for vasomotor symptoms (VMS), particularly if mood symptoms are not present.

**Management of vasomotor symptoms**

HRT is the most effective treatment currently available for the management of VMS of the perimenopause and menopause, improving VMS in at least 90% of women. The actual choice of preparation varies according to the individual woman, her medical history and her personal choice.

There is poor evidence regarding other products such as isoflavones, black cohosh or compounded bioidentical hormones, and the safety of many of these products is still uncertain. Compounded bioidentical hormones are not regulated or licensed and not evidence-based for efficacy and safety.

Testosterone is still not licensed for use in women in the UK. However, it does have a role for those women who still have low libido despite receiving HRT (Achilli et al., 2017). Testosterone can also help to improve mood, energy and concentration (Glaser et al., 2011). Any psychosexual issues should be addressed before prescribing testosterone for low libido. It is important that physiological female doses are used in order to avoid the virilising effects of high doses. Restoration of appropriate female physiological testosterone levels is not associated with significant adverse effects and is supported by the NICE menopause guideline (NICE, 2015a).

**Management of the symptoms of the menopause**

Many clinicians and women understand the benefits of HRT for managing the classic symptoms of the menopause, hot sweats, flushing, tiredness, but may be less good at understanding that HRT can also improve the other symptoms of the menopause. Correcting low oestrogen levels improves the majority of menopausal symptoms and women often find that they feel considerably better within a few months of taking HRT.

**Low mood**

NICE states that healthcare professionals should consider prescribing HRT to alleviate low mood that arises as a result of the menopause (NICE, 2015a). Cognitive behavioural therapy may also be beneficial for some women. There is no clear evidence that antidepressants improve low mood in perimenopausal women who do not have depression, so they should not be used in these situations.

**Urogenital atrophy**

Some women present during or after their menopause with symptoms of urogenital atrophy; one of the commonest symptoms is that of recurrent urinary tract infections with negative urine cultures. These symptoms are often effectively managed by giving women topical vaginal oestrogen.

NICE guidance states that vaginal oestrogen should be offered to women (including those on systemic HRT) with symptoms of urogenital atrophy and then continued for as long as needed to relieve symptoms (NICE, 2015a). A year’s supply of topical oestrogen is equivalent to having one tablet of HRT. This means that vaginal oestrogens can be safely given as a repeat prescription. Women using long-term low dose topical oestrogen do not require progesterone, as there is no endometrial stimulation.

Vaginal moisturisers and lubricants should also be given, either alone or in conjunction with vaginal oestrogen (NICE, 2015a). Moisturisers should be used regularly, as a treatment to rehydrate the vaginal tissues and increase moisture (Edwards and Paray, 2016). Lubricants are recommended prior and during sexual intercourse and do not need to be used on a regular basis. The type of lubricant and moisturiser is important; they should be balanced for pH and osmolality in order to achieve optimum efficacy and to avoid adverse effects.

**Starting HRT**

Women need to be made aware that the HRT benefits and risks vary by dosage, regimen and timing of initiation. They need to be informed that vaginal bleeding may occur in the first 3 months of treatment. The initiating dose should be judged based on the severity of symptoms,
Prescribing HRT

The preparations are usually oral or transdermal and then are sequential or continuous combined. Oestrogen can be given unopposed or combined with a progestogen. Women with an intact uterus need to take oestrogen and progestogen, whereas women who have had a hysterectomy only need to take oestrogen. The Primary Care Women’s Health Forum (PCWHF) has produced a useful flowchart regarding prescribing HRT (Fig. 1).

In general, women who have not had a period for at least a year, and also women who have taken a sequential preparation for at least a year, can be given continuous combined HRT. Taking a continuous preparation means that the women should not have any more periods, although initial breakthrough bleeding is not uncommon.

Benefits of HRT

HRT is often very effective at improving VMS and other menopausal symptoms, including reduced libido. Many women notice their skin, hair, joints and generally well-being also improve dramatically with taking HRT.

Health benefits of HRT

Cardiovascular disease

The risk of cardiovascular disease (CVD) greatly increases after the menopause and CVD is the most common cause of death in women.
worldwide. Studies have shown that there is a lower incidence of CVD in those women who take HRT within 10 years of their menopause. A meta-analysis showed that for women taking HRT within 10 years of their menopause there is a 0.70 relative risk reduction of all-cause mortality and a 0.52 relative risk reduction of coronary heart disease mortality (Boardman et al., 2015).

The CVD benefit of taking HRT is greatest the earlier a woman starts HRT. A large Finnish study has shown that using any HRT for at least 10 years is associated with 19 fewer coronary heart disease (CHD) deaths and seven fewer stroke deaths per 1000 women (Mikkola et al., 2015a).

The NICE guidance states that women should be informed that HRT with oestrogen alone is associated with no, or a reduced, risk of CHD and that HRT with oestrogen and progestogen is associated with little or no increase in the risk of CHD. In addition, the presence of cardiovascular risk factors is not a contra-indication to HRT (NICE, 2015a). It is essential to optimally manage any underlying cardiovascular risk factors (e.g. hypertension, high cholesterol) in women taking HRT. However, having hypertension is not a contra-indication to having or continuing HRT.

This means that having raised blood pressure is not a contra-indication to taking HRT, nor a reason to stop prescribing HRT. Elevated blood pressure should be addressed and promptly managed in women as it is for women who are not taking HRT.

**Osteoporosis**

Fracture incidence increases in women at the menopause, coinciding with lower oestrogen levels, a decrease in bone mineral density (BMD) and higher rates of bone turnover. In the UK alone, annual hospital costs associated with osteoporotic hip fractures are estimated to be £1.1 billion (Leal et al., 2016). The prevention of fractures in postmenopausal women is a vital public health priority worldwide.

Oestrogens are a very effective way of increasing BMD and also preventing osteoporotic fractures in women (Zhu et al., 2016). Consistent evidence from both randomised and cohort studies has demonstrated that the risk of any fragility fracture and non-vertebral fracture is significantly lower for women currently taking HRT (either oestrogen alone or for the combination of oestrogen plus progestogen) compared with non-users (Marjoribanks et al., 2012).

**Dementia**

Some studies have suggested that HRT might impact the risk of dementia, although this requires confirmation (Imtiaz et al., 2017; Mikkola et al., 2017). There is some evidence that there may be a window of opportunity for lowering the risk of dementia with HRT for women with specific preconditions e.g. if they have first-line relatives with dementia, or for women who have premature ovarian insufficiency (Podfigurna-Stopa et al., 2016). NICE recommend that an explanation is given to menopausal women that the likelihood of HRT affecting their risk of dementia is currently unknown (NICE, 2015a).

**Risks of HRT**

Much of the negative publicity surrounding HRT arises from misinterpretation by the media of the findings from the Women's Health Initiative (WHI) study that was published 15 years ago (Rossouw et al., 2002). Many women and healthcare professionals do not realise that many women taking HRT live longer, healthier lives than those who do not take HRT (Anderson et al., 2012).

**Stroke and venous thromboembolism risk**

There is a low risk of stroke and venous thromboembolism (VTE) in women taking oral HRT. The increase in risk of VTE in those taking oral oestrogen is approximately twofold (Oger et al., 2003). This increased risk is far lower than that experienced when taking the combined oral contraceptive pill or with pregnancy. The background risk of VTE increases with increasing age. Women should be made aware that the baseline population risk of stroke in women aged under-60 years is very low.

In contrast, there is no evidence that using standard or low-dose transdermal HRT increases the risk of stroke or of VTE (Canonico et al., 2008). Transdermal preparations of oestrogen should be considered for those women with a higher risk of VTE, including those with a body mass index greater than 30 kg/m² (NICE, 2015a).

**Breast cancer and HRT**

When women are asked about reasons not to take HRT, the most common answer is their concern about the perceived increased risk of breast cancer. Women taking oestrogen-only HRT do not have an increased risk of breast cancer, which is illustrated in Fig. 2. It is only when a progestogen is added to the oestrogen-primed breast tissue that there appears to be an increased risk over a long period of time (Stanczyk et al., 2013). Meta-analysis of the random controlled trial data in the NICE menopause guideline suggests that the excess risk is no more than one extra case per 1000 women per year beyond the average age of menopause (NICE, 2015a). Young women under 51 years in age and taking combined HRT do not have an increased risk of breast cancer.

Epidemiological data support the hypothesis that progestogens are not a uniform class, and that progesterone and progestogens have different effects on the risk of breast cancer in menopausal women using HRT. There is some evidence to suggest that certain synthetic progestogens, such as medroxyprogesterone acetate, may increase breast cancer risk when used in combined HRT and when compared with using micronised progesterone or dydrogesterone (Lyytinen et al., 2009; Fournier et al., 2005). Natural progesterone is micronised, or reduced to tiny particles, and mixed with oil so that it is better absorbed.

An important learning point is that taking HRT does not affect the risk of dying from breast cancer. Women need to be made aware that the increased risk of breast cancer is lower than being overweight or having two glasses of wine each night. Modifiable risk factors for breast cancer, such as obesity, lack of exercise and alcohol intake, should all
be taken into consideration and discussed with a patient. Many women find that their lifestyles improve after taking HRT, so their future risk of breast cancer will actually reduce, despite taking HRT.

**Premature ovarian insufficiency**

Premature ovarian insufficiency (POI) occurs as a result declining ovarian function in young women under the age of 40 years, which leads to a premature onset of menopause. It is a common and an often under diagnosed condition that can have profound physical and psychological consequences without correct management (European Society of Human Reproduction and Embryology, 2015). POI affects around 1 in 100 women under 40 years in age in the UK (Panay and Kalu, 2009).

In the vast majority of cases of spontaneous POI no underlying cause will be identified. Iatrogenic causes include:
- Surgical removal of the ovaries
- Radiotherapy
- Chemotherapy
- Hysterectomy without oophorectomy

This condition should be suspected in any woman who presents with secondary amenorrhoea of more than 3 months' duration. VMS may be present, but around 25% of women do not have symptoms of...
the menopause. Women with untreated POI are at increased risk of developing osteoporosis, CVD and dementia (Podfigurna-Stopa et al., 2016). All these conditions increase the risk of early mortality in these women without treatment.

The diagnosis should be made in women age < 40 years based on (NICE, 2015a):
- Menopausal symptoms, including no or infrequent periods (taking into account whether the woman has a uterus) and
- Elevated FSH levels on two blood samples taken 6 weeks apart

The diagnosis of POI should not be made on the basis of a single blood test. If there is doubt about the diagnosis of POI, women should be referred to a specialist with expertise in menopause or reproductive medicine.

Women with POI should be offered either HRT or a combined hormonal contraceptive, unless contra-indicated. Hormone replacement is important for treating symptoms and protecting against the long-term effects of oestrogen deficiency (European Society of Human Reproduction and Embryology, 2015). There is some evidence that HRT has a more favourable impact on quality of life and bone density than the combined oral contraceptive pill (Cartwright et al., 2016)

NICE guidance is really clear regarding the need for women who have POI to receive HRT until the average age of the menopause (NICE, 2015a). Any risks of HRT are not applicable to these young women; any risks with HRT are only relevant to those women over 51 years of age.

**Summary**
In summary, the NICE menopause guideline should enable clinicians to feel more confident in offering HRT to eligible women. It will also empower women to make more informed choices regarding their treatment, which can now be based on a more balanced review of the evidence. HRT is generally a safe and effective treatment of menopause-related symptoms. All women should be given the opportunity to discuss the pros and cons of HRT and alternatives as they enter the menopause transition. This will empower them to make informed choices about their health at this midlife point and beyond.

**Declaration of conflicting interests**
We have both lectured and acted in an advisory capacity for a number of pharma companies.

**KEY POINTS**
- The mean age of women who have a natural menopause in the UK is 51 years, although there is wide variation between women
- 1% of women experience their menopause before the age of 40 years in the UK
- The menopause is usually a clinical diagnosis based on symptoms in women aged over 45 years
- Topical vaginal oestrogen can safely be prescribed long term for women
- For the majority of women under 60 years in age the benefits of HRT outweigh the risks
- All women with POI need treatment with HRT unless they have contra-indications
A 48-year-old male patient comes to see you requesting screening for chlamydia infection. He is not keen on attending a sexual health clinic.

**What is the specimen of choice to aid diagnosis? Select ONE option only.**

- A. First-catch urine (FCU)
- B. Mid-stream urine (MSU)
- C. Rectal swab
- D. Urethral swab

**Answer:** D. Urethral swab

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**References and further information**


