

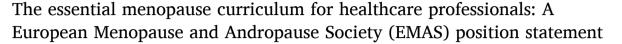
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Position Statement





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ABSTRACT

Introduction: The menopause, or the cessation of menstruation, is a stage of the life cycle which will occur in all women. Managing perimenopausal and postmenopausal health is a key issue for all areas of healthcare, not just gynecology.

Aim: To provide recommendations for the curriculum of education programs for healthcare professionals worldwide, so that all can receive high quality training on menopause.

Materials and methods: Literature review and consensus of expert opinion.

Summary recommendations: Training programs for healthcare professionals worldwide should include menopause and postmenopausal health in their curriculum. It should include assessment, diagnosis and evidence-based management strategies.

1. Introduction

Women's health is increasingly recognized as a global health priority [1]. The menopause, or the cessation of menstruation, is a stage of the life cycle which will occur in all women. The average age at menopause is 51 years. With increasing life expectancy many women will live for several decades after the menopause. However, the menopause can occur much earlier, either naturally, with no identifiable underlying cause [2], or as a consequence of disease, surgery, radiotherapy or chemotherapy. The resulting estrogen deficiency may lead to menopausal symptoms which, for some, can present considerable difficulties in their working lives, discrimination in the workplace and even unemployment [3]. In addition, the conditions associated with menopause and aging such as cardiovascular disease, osteoporosis, dementia and cognitive decline present a considerable challenge to healthcare systems [4]. Thus, managing menopausal and postmenopausal health impacts in all areas of healthcare, not just gynecology.

In 2014, EMAS published guidance on the essential issues that medical students worldwide need to know about reproductive aging, menopause and postmenopausal health [5]. This 2022 curriculum takes into account the 2014 recommendations, new research and new treatment modalities, and is applicable for healthcare education at all levels, including undergraduate, postgraduate and specialist training.

2. Terminology and definitions

Menopause-related terms and definitions are detailed below (Fig. 1) [6,7].

Natural menopause is recognized to have occurred when a woman has had 12 consecutive months without periods (amenorrhea) due loss of ovarian follicular activity for which no other obvious pathological or physiological cause is present and occurs on average at the age of 51 years. Menopause occurs with the final menstrual period and thus is known with certainty only in retrospect one year after the event.

Induced menopause is defined as the cessation of menstruation which follows either surgical removal of both ovaries (with or without hysterectomy) or iatrogenic ablation of ovarian function (e.g. by chemotherapy or radiation). Surgical menopause can be timed precisely.

Premature menopause and early menopause are terms to describe menopause occurring much earlier than the average age of 51 years. Thus, menopause before the age of 40 is commonly referred to as premature menopause, although primary ovarian insufficiency (POI) is currently considered to be a better term to denote the loss of ovarian function, as it does not specify definitive failure. Menopause that occurs between 40 and 45 years is termed early menopause.

Premenopause is a term often used ambiguously to refer to either the 1–2 years immediately before the menopause or to the whole of the reproductive period before the menopause. Currently, this term is recommended to be used in the latter sense, encompassing the entire reproductive period from menarche to the final menstrual period.

Postmenopause should be defined from the final menstrual period regardless of whether the menopause was induced or spontaneous.

Perimenopause includes the period of time beginning with the first clinical, biological and endocrinological features of the approaching menopause, including vasomotor symptoms and menstrual irregularity, and ends 12 months after the last menstrual period. Perimenopause is experienced only with spontaneous (natural) menopause, not induced menopause.

Menopausal transition is the period of time before the final menstrual period, when variability in the menstrual cycle usually is increased.

Climacteric is the phase encompassing the transition from the reproductive state to the non-reproductive state. This phase extends for a variable period both before and after the perimenopause.

3. Curriculum content

The curriculum should cover the following topics and ideally be delivered through lectures and training placements (Fig. 2). If available, teaching should be provided by an accredited menopause expert. The COVID-19 pandemic has increased the use of e-learning for healthcare. This offers some benefits for trainer and trainee; for example, people are not required to travel to attend a training session [8], and recordings can be visited and revisited as required.

3.1. Menopausal symptoms

Vasomotor and urogenital symptoms are the most common symptoms of the menopause. Hot flushes and night sweats affect up to 85% of women and are inappropriate transient episodes of heat loss. They are usually experienced for less than five years, but some women will continue to flush beyond the age of 60 years [9–11]. Although hot flushes and night sweats may begin before periods stop, the prevalence of flushes is highest in the first year after the final menstrual period [9]. Surgically induced menopause through oophorectomy often leads to the immediate onset of vasomotor symptoms. Current smoking and obesity may predispose a woman to more severe or frequent hot flushes.

Symptoms of vulvovaginal atrophy (VVA), which is a component of genitourinary syndrome of the menopause (GSM), are common after the menopause, although they may also occur in pre- and perimenopausal women [12]. They may be lifelong and are experienced by about 50% of postmenopausal women over 60 years of age [13]. Symptoms include dryness, burning, and itching, and dyspareunia may be suffered by both sexually active and inactive women [13]. They can also be associated with urinary tract problems, such as frequent urination, urge incontinence and recurrent urinary tract infections. VVA can have a major impact on interpersonal relationships and quality of life, especially in sexually active women.

Other menopausal symptoms may include chronically disturbed sleep, which, in turn, can lead to insomnia, fatigue, irritability and difficulties with short-term memory and concentration, as well as muscle and joint discomfort [9]. Headaches and migraines may also worsen during the perimenopause.

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Fig. 1. Quick guide to key menopause terms.

3.2. Menopause and long-term health

With rising longevity, there is increasing awareness about long-term health conditions associated with menopause and aging. Cardiovascular disease, osteoporosis and dementia are discussed below.

3.2.1. Cardiovascular disease

Worldwide in 2019 there were approximately 275 million women with cardiovascular disease (CVD), which accounted for 35% of deaths

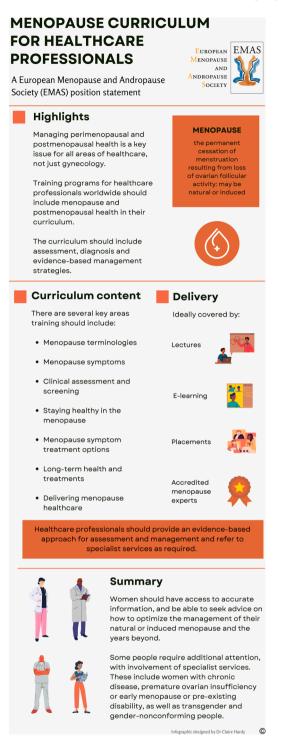


Fig. 2. Menopause curriculum for healthcare professionals.

in women [14,15]. Coronary heart disease and stroke are described below [14].

3.2.1.1. Coronary heart disease (CHD). CHD presents 10 years later in women than in men and symptoms of myocardial infarction may be different in women than in men; as a consequence, women may delay seeking medical assistance. Women are more likely to have non-obstructive CHD than men and have more coronary spasm and/or microvascular disease. The most important preventable risk factors for women developing CVD are poor nutrition, physical inactivity and smoking. Related to these risk factors is the presence of co-morbidities

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such as hypertension, dyslipidemia, diabetes, obesity and psychosocial stress. A history of preeclampsia, gestational diabetes, gestational hypertension, premature menopause and radiation for breast cancer will also increase risk. Women with signs and symptoms of myocardial ischemia who have vasomotor symptoms beginning early in midlife may have higher cardiovascular mortality and reduced endothelial function relative to women with later onset of symptoms.

3.2.1.2. Stroke. Women have strokes at an older age and have a worse prognosis than men. The majority of strokes, 85% in an adult Caucasian population of both women and men, are ischemic. Both intracerebral hemorrhages and subarachnoid hemorrhages are included in hemorrhagic stroke. Around 10% of all strokes are due to intracerebral hemorrhage and 5% due to subarachnoid hemorrhage.

Risk factors for stroke in include: hypertension, atrial fibrillation, smoking, diabetes, obesity, poor nutrition and physical inactivity. The role of hypercholesterolemia in the development of strokes is disputed.

3.2.2. Osteoporosis

One in 3 women and 1 in 5 men over the age of 50 will have an osteoporotic fracture [16,17]. Osteoporosis is defined in a US National Institutes of Health consensus statement as "a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture" [17]. Bone strength reflects the integration of two main features: bone density and bone quality. Bone density is expressed as grams of mineral per unit area or volume and, in any given individual, is determined by peak bone mass and amount of bone loss. Bone quality refers to architecture, turnover, damage accumulation (for example, microfractures) and mineralization.

Fractures of the wrist, hip and vertebrae, which are the main clinical manifestations of osteoporosis, have an enormous impact on quality of life, result in significant economic burden and, particularly in the case of hip fractures, are associated with considerable excess mortality.

The clinical risk factors for fracture include premature ovarian insufficiency or early menopause, increasing age, previous fragility fracture, parental history of hip fracture, current smoking and current glucocorticoid treatment [18].

3.2.3. Dementia and cognitive decline

Worldwide, around 50 million people have dementia, and there are nearly 10 million new cases every year. Alzheimer's disease (AD) is the most common type of dementia, accounting for 60–70% of cases [19]. More women than men have AD or other dementias. Almost two-thirds of Americans with AD are women [20,21]. Other causes include vascular, Lewy body and frontotemporal pathologies. Dementia and cardiovascular disease have many common risk factors, including hypertension, hypercholesterolemia, obesity, and diabetes [20].

3.3. Premature ovarian insufficiency/ early menopause

Premature ovarian insufficiency or early menopause, if untreated, increases the risk of osteoporosis, cardiovascular disease, cognitive decline, dementia and Parkinsonism. The mean life expectancy of women with menopause before the age of 40 years is two years shorter than that of women with menopause after the age of 55 years [2,21,22].

It can either occur naturally, with no identifiable underlying cause [2], or be induced by disease, surgery, radiotherapy or chemotherapy. Ovulation may occur intermittently after diagnosis of POI, possibly resulting in menstrual bleeding and pregnancy, and thus fertility and contraception need to be discussed. In the absence of surgery (bilateral oophorectomy), induced menopause may be permanent or temporary. While some women will wish to have children and need referral for donor oocyte in-vitro fertilization, others will need effective contraception.

3.4. Clinical assessment and screening

Assessment of women seeking advice about menopause should include detailing symptoms and their impact on quality of life and ability to work, menstrual history, type of menopause (natural or induced) and contraception [23,24]. Family and personal history should include that of breast, ovarian, endometrial and colon cancer, venous thromboembolism, migraine, and risk factors for osteoporosis, heart disease and stroke. The women's preference about treatment must be recorded.

Physical examination should include recording of weight, height, waist-hip ratio and blood pressure.

3.4.1. Pelvic assessment and gynecological examination

These should be undertaken in accordance with local guidelines. In general, physical examination and ultrasound, in asymptomatic women, should be restricted to those at high risk of endometrial or ovarian cancer. Abnormal bleeding in the perimenopause or in users of menopausal hormone therapy (MHT) as well as postmenopausal bleeding require evaluation to diagnose or exclude pelvic pathology.

3.4.2. Breast and cervical cancer screening

Women should be encouraged to take part in national screening programs for breast and cervical cancer. In general, more frequent mammography is not recommended in MHT users and the evidence from current randomized controlled trials does not support stopping MHT before mammography to reduce recall rates. Breast examination should be undertaken in accordance with local guidelines.

3.4.3. Osteoporosis screening

In general, population screening for osteoporosis is not advised and, instead, selective examination of high-risk women should be undertaken. Web-based tools for the calculation of fracture risk, such as the FRAX algorithms, can be used to indicate whether women should be referred for dual-energy X-ray absorptiometry (DXA) to assess bone mineral density and need for treatment [25]. The FRAX algorithms give the 10-year probability of hip fracture and of a major osteoporotic fracture (spine, forearm, hip or shoulder fracture).

3.5. Endocrine investigations

3.5.1. Follicle stimulating hormone (FSH)

There is no need to measure FSH levels to diagnose menopause in otherwise healthy women (who are not using hormonal contraception) over the age of 45 who have not had a period for at least 12 months or in perimenopausal women with vasomotor symptoms and irregular periods. Nor should FSH levels be used to diagnose menopause in hysterectomized women with menopausal symptoms aged over 45. However, FSH and estradiol measurements should be undertaken in younger women and considered in those with polycystic ovary syndrome or endometrial ablation, or in women needing a differential diagnosis of amenorrhea [4,24].

3.5.2. Thyroid function tests

Symptoms of thyroid dysfunction can often mimic those of menopause. Thyroid function should therefore be checked when the relevant signs and symptoms are present or when there is a lack of response to MHT [4,24].

3.5.3. Exclusion of other causes of amenorrhea

Pregnancy and hyperprolactinemia need to be excluded, especially in women under the age of 45 [4,24].

3.6. Staying healthy during the menopause

There is increasing evidence that lifestyle factors, such as nutrition,

physical activity, smoking and alcohol consumption, have a profound effect on health and menopause symptoms [26–28]. Women gain on average 10 kg from 40 to 60 years independently of menopause. Thus, women should be supported to stop smoking, address any alcohol dependency, exercise regularly, and to have a plant-based dietary pattern in line with either national dietary guidelines or the Mediterranean dietary pattern, aiming to address health risks, prevent both excess increase in body weight and the anorexia of aging, and achieve a healthy body composition [26,27,29–31].

3.7. Menopausal hormone therapy (MHT)

The fundamental idea of MHT is to replace estrogen. A variety of hormonal preparations are available, each with specific indications, advantages and disadvantages. Different options and combinations are available worldwide.

3.7.1. Types of MHT

The main components of MHT are estrogen and progestogens. Estrogen-alone MHT is given to hysterectomized women. Micronized progesterone or synthetic progestogens are added in regimens for non-hysterectomized women to reduce the increased risk of endometrial hyperplasia and carcinoma which occurs with unopposed estrogen. However, women who take low-dose vaginal estrogen do not need to take a progestogen [13,23]. The routes of administration for estrogen are oral, transdermal (patches, gels and spray), subcutaneous (implants) and vaginal. Progestogens can be administered into the uterus itself with an intrauterine device as well as orally and transdermally. Selective estrogen receptor modulators have been used instead of progestogens for endometrial protection. Note that MHT does not provide contraception unless intrauterine progestogens are used.

Tibolone is a synthetic steroid with estrogenic, progestogenic and weak androgenic activity indicated for the management of menopausal symptoms and urogenital atrophy in postmenopausal women. It does not require the addition of a progestogen in women with an intact uterus [32].

'Bioidentical hormones' is a term used to describe medications which are plant-derived (like approved MHT drugs) and modified to be structurally identical to endogenous human hormones such as estradiol and progesterone. There are concerns about the claims for safety, effectiveness, and superiority of custom-compounded preparations that are not regulated by government agencies (such as the Food and Drug Administration or European Medicines Agency) unlike conventional licensed MHT products [7,33]

3.7.2. Duration of use

Systemic MHT is an effective treatment for menopausal vasomotor symptoms and is usually given for around five years for hot flushes. Topical MHT, however, needs to be taken long term for vulvovaginal atrophy. Systemic MHT also reduces the risk of osteoporotic fracture during treatment but antifracture efficacy decreases once treatment is stopped [4]. Women who experience premature menopause are recommended to take MHT until their early 50 s, not only to treat symptoms but also to reduce the risk of osteoporosis and cardiovascular disease [34]. Thereafter it should be reassessed. It is impossible to predict whether individual women will still be symptomatic or not when they stop systemic MHT. The limited evidence available does not indicate whether it is better to taper down or to stop abruptly, and equally there is no evidence regarding the length of time for which either systemic or low-dose vaginal MHT should be taken. Thus, any limits on duration of use are arbitrary, and treatment should continue for as long as the woman feels the benefits outweigh the risks for her, and decisions must be made on an individual basis [35,36].

3.7.3. Benefits and risks of MHT

The decision to take MHT should be taken in the context of its overall

benefits in terms of symptom management and improving quality of life, as well as improving bone and cardiovascular health. For the majority of women taking MHT, the benefits outweigh the risks, especially for symptomatic women before the age of 60 years or within 10 years after menopause [24,35]. Standard-dose estrogen-alone MHT may decrease coronary heart disease and all-cause mortality in women younger than 60 years of age and within 10 years of menopause. However, initiation of standard-dose oral MHT in women over the age of 60 who have established atherosclerosis may not decrease the risk of coronary heart events. MHT may confer a small increased risk of stroke; there is a suggestion that transdermal preparations have less impact on the risk of stroke than oral preparations. Transdermal estrogen delivery may be associated with a lower risk of venous thromboembolism than oral therapy.

The increased risk of breast cancer in women over 50 years taking MHT is primarily associated with the addition of a progestogen to estrogen therapy and related to the duration of use. It also varies according to the type of progestogen [37]. The risk of breast cancer attributable to MHT is small and decreases after treatment is stopped.

Epidemiological evidence has been inconsistent with regard to risks of developing dementia. A study published in 2021 using a large data sample found that MHT use does not appear to increase the risk of developing dementia overall, but slightly increases the risk of developing Alzheimer's disease among long-term users of estrogen-progestogen therapies [38].

3.8. Non-estrogen-based approaches and therapies for menopausal symptoms

Non-estrogen-based treatments are used to treat hot flushes, symptoms of urogenital atrophy and lack of sexual desire. Both pharmacological and non-pharmacological strategies, but not alternative and complementary therapies, will be described [39,40]. Note that active ingredients in herbal products and dietary supplements can interact with the effect of other medicines [40]. Non-estrogen-based treatments are used in women who do not wish to take estrogens either through choice or because of concerns about comorbidities such as personal or family history of hormone-dependent cancer (e.g. breast cancer) or venous thromboembolism.

3.8.1. Vasomotor symptoms

A variety of agents can be used for hot flushes, including clonidine, paroxetine, citalopram, venlafaxine, desvenlafaxine, gabapentin and pregabalin [39]. These treatments tend to be less effective than systemic estrogens. New pharmacological strategies are in development and currently being assessed in clinical trials [41]. Cognitive behavioral therapy, which can be accessed with self-help books and online, may also help with symptoms [39].

3.8.2. Vulvovaginal atrophy

Many lubricants and vaginal moisturizers are available for use by women experiencing vaginal dryness [13]. Lubricants are typically used episodically to correspond to sexual activity. Moisturizers are usually used on a regular basis, rather than episodically in association with sexual activity. Oral ospemifene and vaginal prasterone (dehydroepiandrosterone) are other options [42,43].

Laser therapy (ablative and non-ablative) for vulvovaginal atrophy or genitourinary syndrome of menopause is a new approach, but large, long-term studies are required to explore its efficacy and safety before definite conclusions can be drawn [44,45].

3.9. Non-estrogen-based therapies for osteoporosis

Treatments include bisphosphonates (alendronate, risedronate, ibandronic acid, zoledronic acid), denosumab, romosozumab, selective estrogen receptor modulators (raloxifene and bazedoxifene) and

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parathyroid hormone preparations (teriparatide and abaloparatide). Women at risk of osteoporotic fracture who take MHT for the management of menopausal symptoms usually do not require additional treatment for osteoporosis. Note that women can take both MHT and non-estrogen-based therapies together for osteoporosis.

Non-estrogen treatments are mainly used in women aged over 60 years because of paucity of data in younger women [17,22]. This also applies for long-term use in women with premature ovarian insufficiency. As the evidence regarding safety on the developing fetal skeleton is unknown, the use of agents which are retained in the body for years, such as bisphosphonates, should generally be restricted to women with no fertility goals.

It must not be forgotten that calcium and vitamin D play a key role in bone health [46,47]. Women may be advised to take supplements if there are dietary deficiencies or if they have very little or no sunlight exposure, especially in autumn and winter.

3.10. Delivering menopause healthcare

Managing menopausal health involves all healthcare professionals, not just gynecologists [48]. During consultations healthcare professionals should take into account that women may have different perceptions and experiences of the menopause, which may be determined by events dating from childhood [49] as well as type and age of menopause. The COVID-19 pandemic has changed the mode of delivering healthcare from face-to-face only to include virtual consultations [50]. Thus, for those who request management of menopausal symptoms, including MHT, full consultations can be undertaken by telemedicine. However, where pathology is suspected, such as postmenopausal bleeding, the virtual consultation to take a medical history will precede in-person investigation and examination.

4. Summary

Managing menopausal and postmenopausal health is a key issue for all areas of healthcare, not just gynecology. Women should have access to accurate information, and be able to seek advice on how to optimize the management of their natural or induced menopause and the years beyond. Some people require additional attention, with involvement of specialist services. These include women with chronic disease, premature ovarian insufficiency or early menopause or pre-existing disability, as well as transgender and gender-nonconforming people. Healthcare professionals should provide an evidence-based approach for assessment and management and refer to specialist services as required.

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