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Menopause Hormone Therapy in 2025

Susan Goldstein, MD, CCFP, FCFP, MSCP

Introduction

Menopause is, in fact, a single day officially marked one year after the cessation of menses. It is followed by post menopause which can last for half of a women's adult life! Menopause typically occurs between the ages of 46 and 52 years with an average age of 51.[1] It signifies the end of reproductive function, and is marked by fluctuating and declining hormone levels, which can lead to a range of often distressing symptoms. The perimenopause is the transition phase that precedes menopause, lasting up to 10 years. For many women, menopausal symptoms may first appear later in the perimenopause. While we use the term "women", guidance applies to all patients who experience menopause, even if they do not identify as a woman.

When people use the term "menopause" they are usually referring to the "climacteric", a period which includes the perimenopause, menopause, and early post menopause stages.

In Canada, over 2.5 million women are between the ages of 45 and 55, and up to 80% of them will experience menopause-related symptoms. There are now over 30 validated symptoms of menopause, some of which can have a significant impact on function and quality of life. A recent study by the Menopause Foundation of Canada reported that up to 10% of women will leave the workforce due to unmanaged menopausal symptoms.[2]

The most impactful symptoms of menopause include vasomotor symptoms (VMS) which include hot flashes and night sweats, sleep and mood disturbances, memory issues, muscle and joint pains, and symptoms of the Genitourinary Syndrome of Menopause (GSM) such as vaginal dryness, bladder issues, and sexual dysfunction. Recent evidence has shown that frequent or severe menopausal vasomotor symptoms are linked to a higher risk for illnesses including cardiovascular disease and diabetes.[3]

The Menopause Quick Six Questionnaire: If a patient answers yes to question 1, they may be perimenopausal or menopausal and further clarification should be obtained. A "yes" to question 2,3, or 4 may indicate symptoms amenable to treatment with Menopausal Hormone Therapy (MHT) or other therapies. A "yes" to question 5 or 6, while not indications for MHT, do indicate relevant symptoms that should be considered when formulating your menopausal treatment plan.

Figure 1. The Menopause Quick Six Questionnaire.[4]; *Reproduced with permissions. Goldstein, Susan. An efficient tool for the primary care of menopause, Canadian Family Physician, April 2017, 63(4):297-298. Accessed April 1, 2025. Available from: https://mq6.ca/mq6-fillable-tool-2/*

Assessing the Need for Menopause Hormone Therapies

Healthcare professionals continue to face challenges with assessing and managing perimenopausal and postmenopausal patients. Lack of time, education, remuneration, and available tools are just some of the obstacles to providing effective care.

Consider starting the discussion about menopause with your patients in their early to mid-40s to help them prepare. A quick and effective approach is to use the Menopause Quick Six (MQ6) assessment tool **(Figure 1)**.[4] Featuring open-ended questions, this tool facilitates conversations and screens for common menopausal symptoms that can be addressed with menopause-specific treatments. A binary-version of the tool can also be found online for patients to self-administer prior to their visit here.

Menopause Hormone Therapies

Menopause hormone therapies include both systemic and local vaginal therapies. The term menopause hormone therapy (MHT), previously known as hormone replacement therapy (HRT), commonly refers to the use of *systemic* hormone therapy.

MHT is indicated to treat VMS, GSM, hypoestrogenic states, and for the prevention of osteoporosis.[1,5,6] Typical MHT regimens include a combination of an estrogen and a progestogen (EPT).

Estrogens provide the main symptom relief from vasomotor symptoms and are available in oral and transdermal formulations (patches and gels). Commonly used systemic estrogens include estradiol (*E2*) and conjugated estrogen. Estetrol, (*E4*) found in a newly developed contraceptive, is being studied for use in MHT.

Progestogens provide uterine protection against estrogen-induced endometrial hyperplasia and include micronized progesterone and synthetic progestins. The 52 mcg LNG-IUS (levonorgestrel containing intrauterine system) may be used *off-label* to safely provide up to 5 years of endometrial protection when used with estrogen in an EPT regimen.[7]

Some women may experience intolerance to progestogenic side effects such as bloating, headache, mood changes, and breast pain. Options include using micronized progesterone vaginally (off-label), long-cycle EPT regimens, and newer products that do not require the addition of a progestogen (i.e., the Tissue Selective Estrogen Complex (TSEC)-CEE/BZA and the Selective Tissue Estrogen Activity Regulator (STEAR)-Tibolone).

Local hormone therapies to treat GSM include vaginal estrogen creams, rings, inserts, and vaginal dehydroepiandrosterone sulfate (DHEAS). A newer oral medication ospemifene, from the class of selective estrogen receptor modulators, has been developed for women who prefer not to use local vaginal products or find it difficult to apply treatments vaginally.

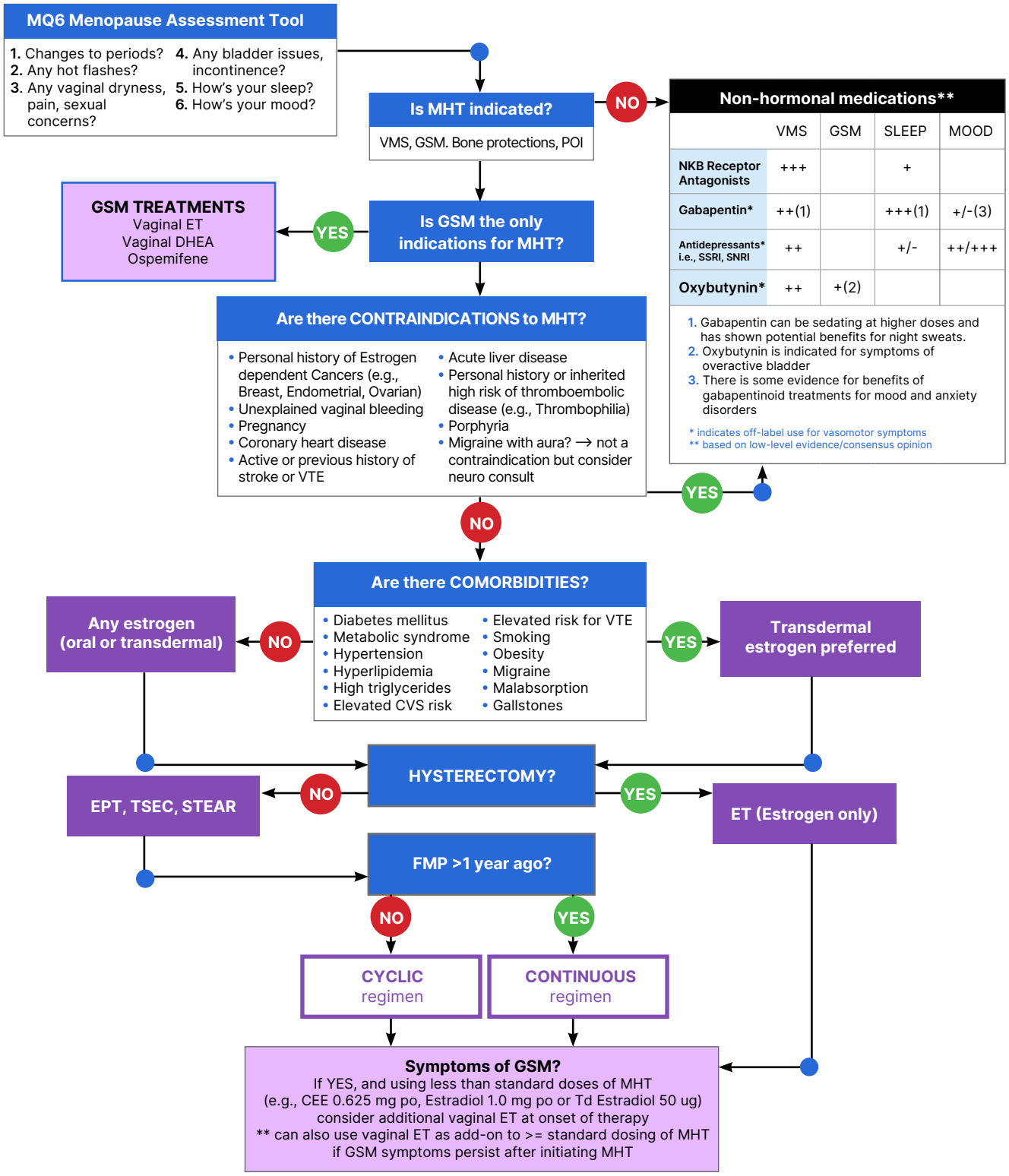

Figure 2. The MQ6 Treatment Algorithm[4]; *Reproduced with permissions. Goldstein S. An efficient tool for the primary care of menopause. Can Fam Physician. 2017; 63(4):297-298. The tool is available from: https://mq6.ca/mq6-interactive-algorithm/#algorithm*

Abbreviations: MHT: Menopausal Hormone Therapy; **EPT:** Estrogen + Progestogen Therapy; **ET:** Estrogen Therapy; **FMP:** final menstrual period **Td:** Transdermal; **POI:** Premature Ovarian Insufficiency; **GSM:** Genitourinary Syndrome of Menopause; **VMS:** Vasomotor symptoms; **TSEC:** Tissue Selective Estrogen Complex; **STEAR:** Selective Tissue Estrogenic Activity Regulator; ***Cyclic regimen:** a daily estrogen with a progestogen added 12-14 days of the month **NKB Receptor Antagonist:** Neurokinin B Receptor Antagonist

Patients frequently request 'bio-identical' hormones, typically referring to custom-compounded hormones. However, their use is discouraged by most menopause guidelines.[1,5,6] For women seeking compounds similar to naturally produced hormones, options such as estradiol, estetrol, and micronized progesterone are considered body-identical.

Tables of products available in Canada can be found in the Canadian Menopause Society Menopause Management Pocket Guide here.

How do the Guidelines Support Management?

After decades of use, the prescribing of MHT halted after the 2002 Women's Health Initiative (WHI) study findings, which reported increased risks of breast cancer, heart disease, and stroke in their cohort. However, these were women aged 50-80 (average age 63) without symptoms, the majority of whom were introduced to MHT after the age of 60 and/or many years post menopause. Two decades of cumulative data since the WHI study,[8] combined with a review of the original findings and recent research, have led to a new understanding of the WHI results, which now guide MHT prescribing in 2025.

National and international guidelines recommend initiating MHT in symptomatic women, without contraindications, who are under the age of 60 or within 10 years of the final menstrual period.[1,5,6]

An Approach to Prescribing MHT: Keeping it Simple

In 2025, the consensus among professional organizations advocates for a patient-centred approach to MHT. This approach begins with a risk assessment to rule out contraindications and to consider comorbidities, demographics, and patient preferences in order to provide an individualized treatment plan.[1,5,6] One approach includes using the Canadian evidence-based MQ6 Treatment Algorithm which supports the healthcare provider in creating a personalized treatment plan **(Figure 1)**.[4,9] The online interactive version of this decision tool can be found at here.

This treatment decision tool starts with reviewing indications for treatment, ruling out contraindications and then considering patient comorbidities to inform choice of regimen. While transdermal estrogens are not preferable for all patients, they are recommended for those with increased cardiovascular or clotting risks, or when timing or absorption may be problematic. The less thrombogenic micronized progesterone is also preferred over synthetic progestins when cardiovascular or breast risks are a concern.[1]

Also consider the reproductive stage, as treatment options differ when initiating therapy in perimenopausal versus postmenopausal women **(Figure 3)**.

Some women are unable or prefer not to take MHT and should be offered non-hormonal treatment options. Recent insights into the pathophysiology of hot flashes has led to the development of a new class of medications indicated for vasomotor symptoms, the Neurokinin B (NKB) Receptor Antagonists, which act locally in the brain, including in the thermoregulatory center, and have shown a reduction in vasomotor symptoms and improved sleep. Fezolinetant is the first-in-class agent from this new class available in Canada.

Other non-hormonal treatment options include the off-label use of SSRI/SNRI's, gabapentin, and oxybutynin, as well as menopause-specific cognitive-behavioural-therapy or hypnosis.[1]

Benefits of MHT

MHT remains the most effective treatment for vasomotor symptoms. In addition to the approved uses (VMS, GSM, bone protection), additional benefits have been reported for mood, sleep, joint pains, and quality of life.[5,6] Twenty years of follow-up after the WHI study provides reassuring evidence for cardiovascular safety.[10]

It is important to inform patients that while MHT can be effective for a number of symptoms, it is not the anti-aging solution they may be seeking. Evidence suggests a "window of opportunity" for cardio-protection when initiating MHT in healthy younger women at low baseline cardiovascular risk. However, guidelines do not support cardiovascular prevention as an indication for MHT.[1,5,6] MHT should also not be prescribed to prevent cognitive decline or dementia and initiating MHT after age 65 may lead to an increased risk of dementia. Although MHT might indirectly help with perimenopausal brain fog, there is insufficient research to support its use solely for this purpose.[11]

Notwithstanding the above considerations, MHT should be prescribed for women

Hormonal Options for Vasomotor Symptoms

Perimenopause

If no contraception required:

1. E + P: cyclic regimen recommended*:
i.e., Estrogen daily + Progestogen Day 1-14

2. Progestogen alone:
e.g., Progesterone 100-300 mg qhs
-less effective for VMS but some sleep benefit

If contraception is required:

3. Estrogen + 52 mcg Levonorgestrol IUS (*off label*)
- Evidence for endometrial protection with the IUS

4. Low dose combined hormonal contraception

*late perimenopause, "off label" when used earlier[1]

Postmenopause

1. E + P: continuous preferred
i.e., daily Estrogen + Progestogen

2. ET (Estrogen alone): if patient has hysterectomy

3. Continuous regimens that don't require the addition of a Progestogen*
a) CEE/BZA
b) Tibolone

*some patients are sensitive to progestogenic side effects such as bloating, headaches, water retention, low mood or somnolence

Figure 3. Hormonal Options for Vasomotor Symptoms; *courtesy of Susan Goldstein, MD, CCFP, FCFP, MSCP*

Abbreviations: E: Estrogen; **P:** Progestogen **ET:** Estrogen Therapy; **VMS:** Vasomotor symptoms

experiencing early menopause and premature ovarian insufficiency. These women are at a heightened risk for bone loss, cardiovascular disease, dementia, and other morbidities, and should be treated up to the natural age of menopause unless there are contraindications. This cohort often requires higher doses of MHT.[5,6]

Risks of MHT

When initiated in women under age 60 or within 10 years of their last menstrual period, the primary risk of MHT is venous thromboembolism (VTE). The highest risk (relative risk,1.74) occurs within the first 1-2 years of treatment.[9] Patients can be reassured that in this cohort, there is no significant increase in the risk of cardiac events or stroke.

The risk of breast cancer is associated with the duration of MHT use, increasing after approximately 5 years of EPT use. This risk may differ based on formulation, dose, mode of delivery, and the presence of and type of a progestogen. The WHI study documented a rare increase in breast cancer risk (<1/1000). While this study reported an increased incidence of breast cancer with the daily use of CEE 0.625 mg + medroxyprogesterone acetate (MPA) 2.5 mg, no increase in breast cancer mortality was observed.[10] This risk is comparable to the increased risk of breast cancer conferred by obesity or alcohol consumption. In contrast, for women using CEE alone, there was a reduction in breast cancer incidence (hazard ratio, 0.78) that persisted after the study ended.[12]

When breast risk is a concern (i.e., positive family history, dense breasts, breast pain) consider the following options which are less stimulating to the breast compared to a standard EPT containing a synthetic progestin. In order of preference these would be: The TSEC (CEE/BZA) followed by the STEAR (Tibolone), followed by EPT containing micronized progestogen.

Duration of Treatment

Vasomotor symptoms last a median of 7.4 years, and in some patients they may persist for 10 years or more. Up to 40% of women will continue to experience vasomotor symptoms into their 60's and 10-15% into their 70's.[1] As such, the duration of treatment should not be fixed, but rather individualized, with a periodic reassessment of indications, patient profile, and risks.

The evidence supports the safe continuation of MHT beyond 65 years when indicated.[13] As women age, switching to transdermal estrogen at the lowest effective dose is advised to help manage the increased cardiovascular risks associated with aging.

Conclusion

As healthcare providers, we need not fear prescribing MHT. Newer tools and research support us in providing a personalized menopause management plan for women with bothersome symptoms, taking into consideration the latest safety information on the multiple treatment options at our disposal.

Keep in mind that menopause represents a time when healthcare risks are evolving. Therefore, it is an important time to remind women about lifestyle changes they can make to optimize their health into the post menopause period of their lives.

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