

GUIDELINE OF THE INTERNATIONAL MENOPAUSE SOCIETY (IMS) DECEMBER 2025 - PART 2

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BACKGROUND

The International Menopause Society (IMS) has developed current recommendations and key messages on the health of women in midlife and menopause based on a comprehensive systematic literature review (1). The aim of these guidelines is to provide healthcare professionals with evidence-based, internationally applicable guidance for the care of women in this phase of life and to support individualized, informed decision-making.

The recommendations cover a broad spectrum, including lifestyle, menopausal symptoms, menopausal hormone therapy (MHT), cardiometabolic health, bone health, cognitive and psychological aspects, and oncological issues. In addition to evidence-based recommendations, good practice points (GPP) and key messages (KM) are also formulated to reflect practice-relevant aspects where data is limited but clinical experience allows for clear guidance.

The IMS guideline uses a transparent rating system based on the GRADE and AGREE II criteria. A distinction is made between two dimensions:

- Quality of evidence (\oplus bis $\oplus\oplus\oplus\oplus$):

This describes how reliable the underlying scientific data is – from very low to high evidence. High evidence means that further research is unlikely to significantly change the assessment.

- Strength of recommendation (A–D):

This indicates how clearly a measure is recommended. In addition to the quality of evidence, it also takes into account clinical benefits, potential risks, feasibility, and patient values and preferences. A strong recommendation (A) can also be made with moderate evidence if the benefits clearly outweigh the risks.

Good Practice Points (GPP) are based on expert consensus in the absence of or insufficient evidence, while Key Messages (KM) represent evidence-based core statements without formulating a specific recommendation for action.

Due to their length, the recommendations will be presented in two newsletters. This is part 2

STATEMENTS

1. Breastcancer

- The overall risk of breast cancer associated with menopausal hormone therapy is low and comparable to or lower than the increased risk associated with common lifestyle factors such as physical inactivity, obesity, and alcohol consumption. $\oplus\oplus\oplus\oplus$ A
- Combined menopausal hormone therapy is associated with an increased risk of breast cancer. This risk increases with the duration of use and gradually decreases after discontinuation of therapy. $\oplus\oplus\oplus$ A
- Sequential combined therapy regimens may be associated with a lower risk of breast cancer compared to continuous combined regimens. $\oplus\oplus\oplus$ B
- Estrogen monotherapy is associated with a lower risk of breast cancer than combined estrogen-progestogen therapy. $\oplus\oplus\oplus$ B
- There is no demonstrable difference in breast cancer risk between oral and transdermal estradiol administration. Similarly, there is no reliable evidence of a dose-dependent increase in risk. $\oplus\oplus\oplus$ C
- In combined MHT, the risk of breast cancer appears to be lower with micronized progesterone or dydrogesterone than with other synthetic progestogens, suggesting a more favorable risk profile. $\oplus\oplus\oplus$ B
- The available data do not indicate an increased risk of breast cancer from vaginal application of hormonal therapies in women without a history of breast cancer. $\oplus\oplus\oplus$ B

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- The use of a levonorgestrel-releasing intrauterine system is not recommended in women with a high baseline risk of breast cancer. ⊕⊕⊕○ B
- Menopausal hormone therapy, including tibolone, should not be used in women with existing breast cancer or in women at high risk of breast cancer. ⊕⊕⊕⊕ A
- No increase in breast density or breast cancer incidence has been observed in postmenopausal women undergoing testosterone therapy; however, there are insufficient randomized long-term data to conclusively assess the risk of breast cancer. ⊕⊕○○ C
- There is no evidence that non-hormonal therapies for the treatment of vasomotor symptoms in breast cancer survivors affect the recurrence rate or breast cancer-specific mortality; they can therefore be used as first-line therapy. ⊕⊕⊕⊕ A
- Vaginal estrogen therapy is effective for treating genitourinary menopausal syndrome in breast cancer survivors and appears to be safe in women undergoing tamoxifen therapy. ⊕⊕⊕○ B

2. Endometrial protection, bleeding management, and diagnostics under MHT

- For endometrial protection, the administration of a progestogen (sequential or continuous) in a monthly dosage proportional to the estrogen dose administered is recommended. ⊕⊕⊕⊕ A
- Women using sequential menopausal hormone therapy should take norethisterone (NET) or medroxyprogesterone acetate (MPA) for a minimum of
 - 10 days of norethisterone (NET) or medroxyprogesterone acetate (MPA) or
 - 12 days of dydrogesterone or micronized progesterone per 28-day cycle. ⊕⊕⊕⊕ A
- Women using adequately dosed sequential micronized progesterone should be informed that there is no evidence of an increased risk of endometrial cancer; however, evidence on use for more than five years is limited. ⊕⊕⊕○ B
- Women over 45 years of age who use sequential MHT should be offered the option of switching to continuous combined MHT after five years or at the latest when they reach the age of 54, whichever comes first. ⊕⊕⊕○ B
- The 52 mg levonorgestrel-releasing intrauterine system (LNG-IUS) provides effective endometrial protection for up to five years at very low to high estrogen doses, both in peri- and postmenopause. ⊕⊕⊕⊕ A
- If irregular bleeding persists for more than six months after starting HRT, diagnostic evaluation and adjustment or modification of progestogen therapy are necessary. ⊕⊕⊕○ A
- Transvaginal ultrasound examination is the first diagnostic measure. ⊕⊕⊕○ A
- With continuous combined HRT, an endometrial thickness of > 4 mm is considered pathological. ⊕⊕⊕⊕ A
- With sequential combined HRT, the endometrial thickness may vary over the course of the cycle. The ultrasound examination should ideally be performed immediately after withdrawal bleeding. If the measured endometrial thickness is > 7 mm, further investigation is indicated. An increased endometrial thickness outside this time window should lead to a repeat examination at a suitable time. ⊕⊕○○ B
- Women with endometrial thickness within the normal range should be reassured and offered adjustment of MHT. If bleeding persists for more than six months despite normal findings, an endometrial biopsy is recommended. ⊕⊕○○ A

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- In cases of pathological endometrial thickness or insufficient visualization of the endometrium, further endometrial diagnostics are necessary. ⊕⊕⊕○ A
- The investigation can be carried out by means of a blind outpatient endometrial biopsy or by means of hysteroscopy with targeted endometrial biopsy. ⊕⊕○○ B
- If irregular bleeding persists three months after a negative blind biopsy, a hysteroscopic examination is recommended. ⊕⊕○○ B
- If insufficient samples are obtained during a blind biopsy, hysteroscopy should be considered. ⊕○○○ B
- If a blind biopsy performed during continuous combined HRT reveals a proliferative endometrium and there are additional risk factors for endometrial cancer, hysteroscopy is recommended. ⊕⊕○○ B
- If unscheduled bleeding persists for more than six months after a previously normal hysteroscopy, further diagnostic investigation should be considered. ⊕○○○ B
- In the event of persistent bleeding under continuous combined MHT, a switch to a sequential therapy regimen should be considered, especially in women in perimenopause. ⊕○○○ B
- A reduction in the estrogen dose should be considered, as lower doses are associated with higher rates of amenorrhea. ⊕○○○ B
- Similarly, an increase in the progestogen dose and/or duration of progestogen use (in sequential therapy) may be considered. ⊕○○○ B
- A switch from micronized progesterone to oral norethisterone acetate (NETA) or MPA may be considered, as these are associated with higher rates of amenorrhea. ⊕⊕○○ B
- If clinically acceptable, switching to oral MHT may be considered, as this can achieve a higher cumulative amenorrhea rate compared to transdermal application. ⊕○○○ B
- If bleeding persists, a dose reduction or discontinuation of MHT should be considered and non-hormonal therapy alternatives offered. GPP

3. Ovarian cancer

- In women with intact ovaries, combined menopausal hormone therapy is associated with a very slightly increased risk of ovarian cancer. ⊕⊕⊕⊕ A
- Even with estrogen monotherapy, women with ovaries have a very slightly increased risk of ovarian cancer, especially when used for five years or longer. ⊕⊕⊕⊕ A
- Menopausal hormone therapy is contraindicated after treatment for epithelial ovarian cancer. Potential risks and possible benefits should be discussed individually with the women concerned. ⊕⊕⊕○ A
- Although the majority of high-grade serous and endometrioid ovarian cancers express the estrogen receptor, the currently limited randomized study data do not indicate an increased risk of recurrence under systemic MHT. Nevertheless, it may be advisable to offer non-hormonal therapy options first, especially in women without premature or early menopause. ⊕⊕⊕○ B

4. Lung cancer

- The available evidence on the link between menopausal hormone therapy and lung cancer is inconsistent; to date, no clear influence of MHT on the incidence or mortality of lung cancer has been demonstrated. KM
- Women diagnosed with lung cancer who benefit clinically from menopausal hormone therapy do not necessarily have to discontinue MHT, as the available data show no adverse effects on survival time and, in individual analyses, even suggest a possible survival benefit. ⊕⊕⊕○ B

5. Colorectal cancer (CRC)

- The lower incidence of colorectal cancer in women compared to men could be due to the protective effect of estrogens. KM
- A possible protective role of menopausal hormone therapy was supported by the results of the combined estrogen-progestin group of the Women's Health Initiative (WHI) and corroborated by a comprehensive umbrella review. The observed protective effect decreased over time and did not achieve a statistically significant reduction. In addition, there was no reduction in colorectal cancer-specific mortality. ⊕⊕⊕○ B

6. Cervical carcinoma

- Menopausal hormone therapy may be considered for symptomatic women with HPV-independent cervical cancer, especially for women who have developed premature or early menopause as a result of oncological treatment. Due to the limited evidence on safety in this patient group, careful individual risk-benefit assessment is recommended. If the risk constellation is unclear, non-hormonal therapy options should be preferred. ⊕⊕⊕○ C

7. Malignancies of the upper gastrointestinal tract

- Menopausal hormone therapy could have a potential benefit in slowing the progression of early stages of hepatocellular carcinoma, thereby possibly contributing to an improvement in treatment outcomes. However, the available evidence is limited. ⊕⊕⊕○ C
- Observational studies suggest that menopausal hormone therapy may be associated with a reduced risk of gastric cancer in postmenopausal women; however, a causal relationship cannot be definitively established. ⊕⊕○○ C
- For esophageal cancer, the evidence regarding the protective effect of menopausal hormone therapy is inconsistent. Individual studies provide evidence of a possible protective association in adenocarcinomas, but the data remain limited. ⊕⊕○○ C

8. Mental health, cognition, and sleep during menopause

Anxiety disorders

- The effects of menopausal hormone therapy on anxiety disorders are currently not sufficiently clear. ⊕⊕○○ C
- There is insufficient evidence to recommend the use of menopausal hormone therapy for the treatment of anxiety symptoms in peri- or postmenopausal women. ⊕⊕○○ C

Cognitive function

- With the exception of women with premature ovarian failure or early menopause, menopausal hormone therapy is not recommended at any age for the prevention or treatment of cognitive impairment. ⊕⊕⊕⊕ A
- In natural early postmenopause, menopausal hormone therapy has no demonstrable effect on cognitive abilities. ⊕⊕⊕⊕ A
- A possible cognitive benefit of menopausal hormone therapy has been described when initiated immediately after hysterectomy with bilateral oophorectomy. ⊕⊕⊕○ B
- The effects of menopausal hormone therapy on the cognitive abilities of women with moderate to severe vasomotor symptoms and women in perimenopause have not yet been sufficiently studied. KM

Depressive symptoms

- There is evidence that estrogen monotherapy (ET) can improve anhedonia in perimenopausal women without depressive disorder. Whether ET generally improves depressive symptoms in this population has not been conclusively clarified. ⊕⊕○○ C

- ET may improve depressive symptoms in perimenopausal women with depressive disorders, regardless of the presence of vasomotor symptoms. Its efficacy in this population appears to be comparable to that of antidepressants. ⊕⊕○○ C
- In postmenopausal women without depressive disorder, ET may contribute to the alleviation of depressive symptoms. ⊕⊕○○ C
- HRT is not effective for treating depressive symptoms in postmenopausal women with diagnosed depression. ⊕⊕○○ C
- Menopausal hormone therapy could potentially reduce the occurrence of clinically relevant depressive symptoms in euthymic women during menopause; however, the current evidence is insufficient to make a recommendation. ⊕⊕○○ C
- HRT may enhance the clinical efficacy of antidepressants in perimenopausal women with vasomotor symptoms. ⊕⊕○○ C

Sleep

- Menopausal hormone therapy improves sleep in women with vasomotor symptoms, but has no consistent effect on the sleep of menopausal women overall. ⊕⊕⊕○ B
- Transdermal estrogen may improve sleep quality in perimenopausal women, even beyond its effect on vasomotor and other menopausal symptoms. ⊕⊕○○ C
- Micronized progesterone taken before bedtime may improve various sleep parameters in postmenopausal women. ⊕⊕○○ C
- Cognitive behavioral therapy for insomnia (CBT-I) is recommended as first-line therapy for sleep disorders in menopause. ⊕⊕⊕A

9. Androgens, testosterone, and DHEA in women

- Available studies show that serum testosterone concentrations decline continuously during the reproductive phase of life, do not change abruptly with the onset of natural menopause, and rise again from the seventh decade of life onwards. In contrast, serum DHEA levels decline continuously with age. ⊕⊕⊕○ B
- The majority of currently available immunoassays are not sufficiently accurate to reliably measure testosterone concentrations in the female reference range. In addition, the reference ranges vary considerably between test methods. There is no defined serum testosterone threshold below which testosterone deficiency can be diagnosed in women. ⊕⊕⊕⊕
- Postmenopausal hypoactive sexual desire disorder (HSDD) is an evidence-based indicator for a therapeutic trial with physiological doses of testosterone. ⊕⊕⊕⊕ A
- Before prescribing testosterone, all women with sexual dysfunction should undergo a comprehensive biopsychosocial assessment, and potentially modifiable factors should be addressed. ⊕⊕⊕⊕ A
- The available evidence does not support prescribing testosterone to women for the treatment of symptoms or conditions other than postmenopausal HSDD or for the prevention of disease. The quality of evidence ranges from ⊕⊕⊕○ B to ⊕⊕⊕⊕ A
- Current evidence does not support the use of systemic DHEA therapy for the treatment of sexual function changes or other clinical symptoms or conditions in women. ⊕⊕⊕○ B
- Intravaginally administered DHEA (prasterone) is an effective treatment option for dyspareunia resulting from genitourinary syndrome of menopause (GSM). ⊕⊕⊕⊕ A

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(1) Panay N, Fenton A, Hamoda H, Hillard T, Islam R, Pedder H, Romero L, Vincent AJ; (IMS Publication Steering Committee) and The IMS Recommendations Writing Group; IMS Recommendations Writing Group;

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