MENOPAUSE MATTERS

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The Status of menopause hormone therapy (MHT) in the United States (USA)

Much of menopausal medicine depends on the status of MHT. Its place in the armamentarium of those working in this domain will dictate the enthusiasm with which they can recommend and prescribe hormone treatment.

USA Hormone History

Historically, in the USA at least, the role of "Hormone Replacement Therapy" was overplayed, then reversed by the *Women's Health Initiative* research study by an ultra-conservative clinical approach until re-examination of the data, which gave different insights into some aspects of its controversial outcomes.

At the turn of the century in the USA, 25% of eligible women were on systemic hormone therapy, but the WHI study outcome reduced this number to 5%. This was far fewer than needed treatment for their symptoms, but fear of litigation should detrimental effects occur, dissuaded doctors from prescribing hormones, and much of the world followed suit. Another factor that held sway in the US was the package insert information that accompanied each prescription which included a "Black box" warning. It was a full warning of serious risks such as cardiovascular disease, thromboembolism, breast cancer, and probable dementia. These warnings, however, did not stratify risk by age of initiation or formulation type. Thus, topical estrogens for local vulval and vaginal purposes – apart from other systemic medications – were "tarred with the same brush" and the result was fear and alarm.

The American Federal Drug Administration (FDA) failed to revise these warning labels for 20 years, despite newer medications, various routes of administration and research showing completely different risk profiles for topical and systemic preparations. There were serious requests to have the situation reviewed, with fresh evidence, delegations and repeated requests to the FDA, emphasising alterations to the drugs offered and their safety.

Political clouds

However, the situation in the US is not necessarily driven by evidence-based logic. There are powerful ideological considerations and blatant politically logs in the road to be negotiated by anyone wishing to introduce new concepts – no matter how they may be in keeping with the majority's interests and wishes. Examples of counter intuitive law-making against the health interests of many are:

- Last year the administration introduced laws described as "The Worst Piece of Health Care Legislation Ever" (Cutler. *JAMA Health Forum*. 2025; doi:10.1001/jamahealthforum.2025.4626)
- The Supreme Court's 2026 Term—Public Health in Jeopardy (Gostin. *JAMA Health Forum*. 2026; doi:10.1001/jamahealthforum.2026.0061) speaks to the partisan rather than scientific currents that steer health-care in modern America.
- Two thirds of Americans believe abortion should be "legally available in all or most cases" AP-NORC survey. 2025, yet a large number of States make abortions illegal.

The "Black box warnings" removed

Against this unpredictable and disruptive background, the FDA's decision to rescind the package insert "Black box warnings" on estrogen-containing products came as a welcome development. This will allow US citizens to make more informed decisions and free-up prescribers not to excuse or gain-say the package labelling. It should also encourage others with midlife women's health interests at heart to open conversations in their favour and this decision marks a significant shift in prescribing practices.

Editorial comment: Please note the SAMS statement which explains that the removal of the black box warning on low-dose local vaginal estradiol is very welcome but the wholesale removal of the black box warning from systemic estrogen products should use a nuanced approach, "…based on current available evidence, …when initiating systemic MHT, as a wide range of formulations containing different oestrogens and progestogens/progesterone are available. Care should be taken not to overstate benefits or minimise possible risks." https://www.menopause.co.za/wp-content/uploads/2026/01/South-African-Menopause-Society-SAMS-Response-to-FDA-Removal-of-Black-Box-Warnings-on-Menopausal-Hormone-Therapy-MHT.pdf

Expert reactions

The reaction of experts in the field has been positive. An article summarises measured responses from JoAnn Manson, Stephanie Faubion and Laure-Anne Teuwen (Evangelou. *Medscape*. 2026). They agree that nuanced prescribing in conjunction with the patient's participation is now more likely since the "authorities" and medical experts are no longer in disagreement.

Much of what these experts discuss is the role of MHT in relation to the risk of breast cancer. Evidence from randomised controlled trials and observational studies demonstrates that combined estrogen-progestogen therapy (EPT) increases breast cancer incidence, with risk rising alongside duration of use. However, estrogen-only therapy shows a protective effect. The WHI trial found EPT increased breast cancer risk (HR 1.28), whilst estrogen alone reduced it (HR 0.78). Despite increased availability of products that no longer contain medroxyprogesterone acetate, long-term mortality data remains uncertain. It is postulated that, based on observational studies of newer formulations such as micronised progesterone, the new drugs will pose less of a risk of breast cancer than medroxyprogesterone acetate.

Absolute risk increases are modest—approximately one additional case per 1,000 women annually with combined medications, comparable to lifestyle factors such as "one to two glasses of wine per night, as having overweight or obesity, or as being inactive." Significant research gaps persist regarding newer formulations, particularly transdermal estradiol and micronised progesterone, with experts calling for large-scale trials comparing contemporary regimens.

The evidence regarding the effect of MHT on breast cancer mortality is conflicting, with the early data from the WHI trials demonstrating that deaths directly attributed to breast cancer were greater in the EPT group than in the placebo group (0.03% vs 0.01% annualised mortality rate).

These findings contrast with more recent WHI analyses, which showed that after long-term follow-up of the WHI CEE plus MPA trial, there was no significant difference in breast cancer mortality. These early WHI findings may have been influenced by the shorter follow-up period and fewer events, which may have contributed to discrepancies between the early data and long-term follow-up data.

"Variation in findings across different studies can be explained by differences in study design, population characteristics, MHT regimens, timing and duration of therapy, and confounding factors such as mammography frequency and underlying breast cancer risk," Teuwen said.

“Breast cancers diagnosed in MHT users tend to be detected at an earlier stage, partly due to increased mammography screening,” she said. She added that the majority of MHT-associated breast cancers are hormone receptor-positive, which generally have a more favorable prognosis.

Information needed

Specifically, data are needed on the breast cancer risks of today’s products. “We need to better understand the safety profile of the commonly used hormone therapy regimens we have today and how they differ from what was used previously,” one expert stated. Another said there was the need for large, multicenter RCTs directly comparing contemporary MHT formulations to placebo. She added that “trials should include stratification by baseline breast cancer risk and use standardized mammography protocols to minimize detection bias. In addition, trials should enroll women at the typical age of MHT initiation (eg, aged 50-54 years) and include long-term follow-up of at least 10-20 years to capture both incidence and mortality outcomes, along with detailed collection of tumor subtype and receptor status.”

The likelihood of such a trial over two decades is remote, so careful observational studies may be the best option in formulating breast cancer risks.

Editorial opinion. Perhaps part of the answer will be provided by better genetic risk profiling in candidates for MHT. Also, far more accurate screening processes, possibly in the form of liquid biopsies need to be explored, so that prediction and reliable early warning diagnostics will provide acceptable risk scores. Is this a field in which AI will provide a break-through?

Reconsidering Hypoactive Sexual Desire Disorder

Flibanserin has recently been approved by the FDA of America for the treatment of hypoactive sexual desire disorder (HSDD) in postmenopausal women up to age 64 years. It was previously approved for use in premenopausal women based on existing studies conducted prior to flibanserin’s original approval.

Evidence of the medications effectiveness was reviewed in 2024 when it was deduced that using the active drug, postmenopausal women experienced 0.4 more satisfying sexual events per month than when using placebo (Kamrul-Hasan et al. *Medicine (Balti).* 2024; doi:10.1097/MD.0000000000038592). Besides flibanserin’s contraindications concerning alcohol co-consumption being somewhat relaxed, other restrictions remain in place.

Editorial opinion. Medications should not be the first line of action in the treatment of HSDD disorder at any age. If drugs are considered, then cost and effectiveness must be taken into account. Whether one third more of a satisfying sexual event per month (than taking a placebo) constitutes clinical significance will be at the discretion of the prescriber, as will the cost of the drug chosen. In the case of flibanserin this “is estimated to be $1100 per month” (Haelle. Medscape. 2025).

Information about testosterone as an evidence-based therapy for lessened libido is available (Sharon et al. Menopause. 2023; doi:10.1097/GME.0000000000002190).

Editorial comment: Testafeme, which contains the appropriate level of testosterone for midlife women, has been approved by SAHPRA and may be be prescribed for HSDD. The testing recommendations cited should be followed.

Complementary Therapies for Management of Menopausal Symptoms:

Menopausal hormone therapy is the most effective treatment for menopause symptoms, but many women also use complementary therapies alongside conventional care. A review has summarised the available research on different complementary therapies used by women during and after menopause (Maunder et al. *Climacteric*. 2026; doi:10.1080/13697137.2025.2584061).

Overall, the quality of these trials and reviews was low.

Many complementary therapies showed promising results, such as acupuncture, Chinese herbal medicine, herbal medicines, vitamin and nutrient supplements, and mind-body approaches; however, most are supported by low-quality evidence. The strongest evidence supported the safety of vitamin D, while moderate evidence suggested benefits from black cohosh for hot flushes and menopausal scores; Chinese herbal medicine for menopausal scores, sleep quality and blood pressure; acupuncture combined with Chinese herbal medicine for sleep quality; and vitamin D for reducing fracture risk.
In summary, complementary therapies including vitamin D, black cohosh and Chinese herbal medicine may help some menopausal symptoms, but more high-quality research is needed to understand how effective and safe these treatments truly are. In general, most complementary therapies appeared safe, with few serious side effects reported. However, more high-quality research on complementary therapies is required to confirm the benefits and risks to menopausal women.

Editorial comment. This summary was computer generated.

Note: The new IMS recommendations for MHT initiation and use, including key messages on women's midlife health and menopause, are now available with a comprehensive section on non-hormonal treatements, including complementary and herbal supplements for VMS: Panay N, et al (IMS Publication Steering Committee) and The IMS Recommendations Writing Group; Climacteric. 2025 Dec;28(6):634-656. doi: 10.1080/13697137.2025.2585487. Epub 2025 Dec 23. PMID: 41433054.

Consolidation After Osteoanabolic Therapy - A Cohort Study

A large US study examined practices following osteoanabolic therapy amongst women with a mean age of 72 years. Participants had low bone mineral intensity measurements with half having experienced previous fractures. For optimal ongoing protection from osteoporotic disadvantage, consolidation therapy with antiresorptive medication should be instituted within three months of completing anabolic treatment (Badour et al. *JAMA Intern Med*. 2026; doi:10.1001/jamainternmed.2025.7530).

In the cohort followed-up in the above article, less than one third received timely consolidation treatment. Where this was prescribed, teriparatide was the most commonly used medication.

Editorial comment: Despite guideline recommendations emphasising timely consolidation to preserve bone mineral density gains and reduce fracture risk, substantial gaps persist between recommendations and clinical practice, warranting interventions to improve post-anabolic management.

Rapid information snippets

There were a number of articles that appeared last year that might not have received prominence. Your editor is therefore itemising some that may catch your eye:

- **A novel non-hormonal treatment for menopausal symptoms.**

Effect of a novel nutraceutical combination of EstroG-100 and γ-aminobutyric acid (GABA) in attenuating symptoms of menopause in healthy adult women: a randomized double-blinded placebo-controlled study by Snigdha et al. *Menopause.* 2025; doi:10.1097/GME.0000000000002608

The authors' conclusion was that "The novel nutraceutical combination of Estro-G100 and GABA may help support women during menopause."

- **Associations' guidelines to GSM strategies**

The AUA/SUFU/AUGS Guideline on Genitourinary Syndrome of Menopause by Kaufman et *al. J Urol.* 2025; doi:10.1097/JU.0000000000004589 and Rubin et al. *Medscape*. 2025

These strategies were evidence-based and consensus statements that allow symptoms to guide hormonal therapies at the clinicians' discretion.

- **Exercise for treating menopausal sleep issues**

Menopause and movement: exercise for better sleep and psychological well-being—a systematic review by Choudhary et al. *Menopause*.2025; doi:10.1097/GME.0000000000002610

- **Weight-loss medications and MHT**

GLP-1 Weight Loss in Postmenopausal Women Greater With Hormone Therapy by Haelle. *Medscape*. 2025. Research presented at last year's Menopause Society's Annual Meeting stated that "postmenopausal women taking menopausal hormone therapy had the greatest weight loss"

And at the same meeting data showed *that "Transdermal Menopausal HT Linked to Fewer Anxiety, Depressive Symptoms Than Oral HT"* by Haelle. *Medscape*. 2025

Women who used transdermal hormone therapy to treat menopausal symptoms experienced lower rates of anxiety and depression than those who used oral HT.

- **Hysterectomy approach for benign indications**

Vaginal hysterectomy vs laparoscopic hysterectomy for benign indications: complications and length of stay in a national analysis of contemporary data by Meyer et al. *AJOG*. 2025.

There was little to choose between the two techniques in terms of complications (around 7%) and vaginal hysterectomy offered shorter operative times, but longer hospital stays. Overall, there was no clear advantage so preferences can be really competitive

- **Screening for colorectal malignancies**

Almost all patients consulting those who specialise in menopausal medicine should have routine screening for colorectal cancer. The faecal and direct visual scoping methods are well described but blood-based (liquid biopsies or tumour DNA tests) are gaining momentum as clinically reliable alternatives. Two articles give informative data about these developments:

Clinical Validation of a Circulating Tumor DNA–Based Blood Test to Screen for Colorectal Cancer by Shaukat et al. *JAMA.* 2025. doi:10.1001/jama.2025.7515

An Exosome-Based Liquid Biopsy for the Detection of Early-Onset Colorectal Cancer: The ENCODER Multicenter Study by Mannucci et al. *Gastroent*. 2025; doi:10.1053/j.gastro.2025.08.013

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