MENOPAUSE MATTERS
OCTOBER 2025

Menopausal Hormone Therapy – risks & benefits

Last month's *Menopause Matters* lead item was concerned with reflections on the Women's Health Initiative (WHI) trial and the resounding impact it had on the health of older women for the next 20 years, with unexpected consequences for their short and long-term wellbeing.

The drugs investigated turned out to be unfortunate choices – although they were popularly prescribed at the time – and the participants recruited proved to be too wide an age group from which to draw conclusions that could apply to individual women past their menopause transition.

The deleterious effects described, plus the press abreaction were destined to retard using or interrogating menopausal hormone therapy for a long time. There was administrative over-reaction with the Food and Drug Administration of America embarking on a range of proclamations and "black-box" warnings that have persisted for decades and discouraged appropriate menopausal hormone use.

Clarifications and re-examination of the data have provided valuable insights into which compounds are safe, and which are not, as well as to whom, and when they should be prescribed. There were certainly "important negative findings" revealed, and the prescription or over-prescription of potentially harmful medications was halted. However, this "swing of the pendulum" to the negative side has proved difficult bring back to an evidence-based norm.

On 27th October this topic was addressed by experts (Thurston & Huang. *JAMA. Intern Med***.** 2025 doi: 10.1001/jamainternmed.2025.5340) who make the point that "Women comprise over half of the world's population and will spend almost half of their lives in their peri- or postmenopausal years. Most women will have menopausal symptoms, with a varying degree of impact on quality of life, and many may benefit from menopause care. The field must evolve beyond its polarized positions about MHT".

Polarised positions taken up about menopausal hormone therapy are being lessened by evidence that the three domains of its use are all refining the parameters within which they are effective and safe for:

- Relief from bothersome perimenopausal symptoms at the time of the menopause transition
- Their likely association with long-term health
- Topical or local use for remediation of the genitourinary syndrome of menopause (GSM)

Perimenopausal symptoms at the time of the menopause transition

Most menopause societies and academic sources now clearly recommend systemic estrogens (and progesterone) as the method of choice in treating bothersome vasomotor and related symptoms arising in the perimenopause. This is with the proviso that there are no contra-indications and decisions are made jointly with professional guidance and the patient.

Present-day medications and their route of administration are less likely to cause adverse effects, and their components are considered safe. There is general agreement on this score.

Newer data suggests it is likely that there will be advantages of combination use over a decade, as described in large studies from the US such as the analysis of prescription and health records of 10 million women to assess MHT use beyond 65 years (Baik et al. *Menopause*. 2024; doi:10.1097/GME.0000000000002335).

This research found that estrogen monotherapy beyond age 65 showed significant risk reductions compared to never-use or discontinuation: 19% lower mortality, 16% reduced breast cancer, 13% lower lung cancer, 12% reduced colorectal cancer, plus reductions in cardiovascular diseases and 2% lower dementia risk.

Combination estrogen-progestogen therapy results varied by type. Estrogen + progestin increased breast cancer risk by 10-19%, though low-dose transdermal or vaginal formulations mitigated this risk. Estrogen + progestin significantly reduced endometrial cancer (45%), ovarian cancer (21%), and several cardiovascular conditions (5% each). Estrogen + progestin showed a reduction in congestive heart failure (4%). Overall, benefits were greatest with low-dose, transdermal/vaginal preparations using estradiol rather than conjugated estrogen or oral routes.

Editorial comment. These data can only be considered in the clinical context, if:
The person has initiated MHT soon after the menopause transition and below the age of 60 years
She has no contraindications to its use
The medication has been prescribed for her by a registered medical practitioner who is responsible for her safe continued use of what is prescribed.

Your editor is strongly in favour of MHT and will continue to call for is wider application because it has acquired an unfortunately negative reputation in the past. However, the swing of the pendulum needs responsible handling lest it moves to a point where MHT reinvents itself as a panacea for ageing. This is especially important as the social media and other information platforms enjoy high-profile news items, and these can be "clutched-at" in good faith but misguidedly so.

An example is the value of MHT for Alzheimer's protection. It is not medication that can reverse the condition and its effect on prevention – even with modern medications – is not clinically statistically significant. For a clear and entertaining podcast on the topic please click on:

https://www.instagram.com/reel/DQ90hhoASo5/?igsh=YzRtaWV0a3YwZ2Js

It is your Editor's opinion, that topical (vaginal) estrogen containing creams should be available over-the-counter and be dispensable by pharmacists. Please note the disclaimer clause at the end of this newsletter!

As wider and longer use is reported, there may be "spin-off" advantages. One such example is the synergistic effect of latest weight-loss drugs with MHT that has been suggested by tirzepatide experiments recently presented (Haelle. *Medscape*. 2025). Another is the report indicating that MHT may have a protective effect against upper GIT cancers (McCall. *Medscape*. 2025).

Changes in United States MHT labelling

The US Food and Drug Association has recently revised (as of July 2025) its stance about warnings on many MHT products. The alterations to the US range of hormone package inserts reflects modern MHT risks, especially about initiation, administration, duration and topical MHT use. (Makary et al. *JAMA.* 2025; doi:10.1001/jama.2025.22259).

Editorial opinion.
Dr Makary's association, given in the article summarised above, is "US Food and Drug Administration".

This publication comes at a time of political disruption of the American healthcare system.
Doctors and their professional organisations find themselves in conflict with governmentally appointed persons who express views that are not congruent with accepted medical science in the fields of medical insurance, public health, immunisation and drug regulations.

The MHT relabelling decisions are welcomed by medical practitioners around the world as out-dated restrictive legislation in the dispensing of drugs in America can influence the position taken by other countries.

This latest announcement will hopefully send a message of progressive thinking that reflects the views of those societies acting in women's best interests.

It is of note that the increased risk in breast cancer cases observed in the original WHI study has been subsequently attributed to the progestogen formulation used in the study, medroxyprogesterone acetate. More modern progestogens appears to have lesser carcinogenic effects but the increased risk of breast cancer from the use of MHT remains a risk factor. This should be taken into account in nuanced discussion between the patient and the professional prescribing such medication.

MHT for breast cancer patients: what is the current evidence?

The risks of using MHT in breast cancer survivors is controversial with empirical evidence needed and called for. The latest view is expressed by a 25-member multidisciplinary expert panel which developed a set of consensus statements concerning Menopausal Hormone Therapy for breast cancer patients (Glynne et al. *Menopause.* 2025; doi:10.1097/GME.0000000000002627).

"Many breast cancer survivors struggle with menopausal symptoms due to oncological treatment-induced hormone deficiency, or because they experience menopause some years after completing treatment, but have limited menopause treatment options. Estrogen replacement therapy is the most effective treatment for menopausal symptoms, but is not recommended after breast cancer because it can increase the risk of relapse." This is not empirical research but a consensus statement that will be of use to all practitioners and patients wishing to define the role of menopausal hormone therapy after breast cancer.

Their findings were as follows: "The panel agreed that some women may choose to take MHT, (off-label use) and accept an increased risk of relapse in exchange for relief from menopausal symptoms and an improved quality of life, and that preferences may vary according to individual circumstances and the absolute risk of relapse. All respondents agreed or strongly agreed with statements supporting shared decision making and individualized menopause care".

"In our review of the literature, we found mainly moderate quality evidence concerning use of vaginal and systemic estrogen after breast cancer, and high quality evidence concerning the benefits of anti-estrogen therapy for estrogen receptor positive breast cancer. Based on the available data, we recommend that shared decisions are based on (1) an individual's menopausal symptoms and impact on quality of life, (2) the potential increase in an individual's risk of relapse by use of menopausal hormone therapy, and (3) patient preferences, views and treatment goals. Clinicians and patients can use our findings to make informed menopause treatment choices after breast cancer."

"We strongly recommend registering all patients considering MHT after breast cancer in a clinical study (eg, MENopausal hormone therapy and Outcomes After Breast Cancer, the MENO-ABC trial)."

Topical use for remediation of the Genitourinary Syndrome of Menopause
It is your Editor's opinion that topical hormonal therapy for the treatment of the GSM is the most under-utilised medication in women.

It has the potential to treat

- Vaginal dryness, burning, and irritation
- Dyspareunia
- Urinary urgency, frequency, and recurrent infections
- Changes in vaginal pH and the flora of the genital tract (Da Silva et al. *Front. Cell. Infect. Microbiol*. 2025; doi:10.3389/fcimb.2025.1595182)

More than half of all women surveyed admit to genitourinary symptoms postmenopausally, but the topic is under-reported and under-treated (Da Silva et al. *Fac Revs*. 2021; doi:10.12703/r/10-25).
It is safe in that there is:

Minimal systemic absorption: Low-dose vaginal estrogen results in minimal to no increase in serum estrogen levels, keeping them within the postmenopausal range
No increased endometrial risk: Unlike systemic estrogen therapy, low-dose vaginal estrogen does not require concomitant progestogen therapy because it does not cause endometrial proliferation or increase endometrial cancer risk
No increased cardiovascular or thromboembolic risk: The minimal systemic absorption means no increased risk of blood coagulation, stroke, or cardiovascular events
No increased breast cancer risk: Current evidence does not show an association between low-dose vaginal estrogen and increased breast cancer risk

The following organisations recommend vaginal estrogen as first-line therapy for GSM: The Menopause Society, American College of Obstetricians and Gynecologists & The International Menopause Society.

Urinary tract infection symptom management in postmenopausal women has been reviewed, and it was found that there is a dearth of guideline concordant care advice relating to estrogen use (Bradley et al. *Menopause.* 2025; doi:10.1097/GME.0000000000002609).

Editorial comment. The preceding concentration on hormonal solutions needs to be balanced by "other options", some of which could be considered unusual – very unusual – so read on in wonder!

Hot flushes helped by wrist cooling?

A crossover trial has investigated whether a wrist cooling device could reduce hot flushes in cancer patients and postmenopausal women. A small group of patients experiencing frequent moderate-to-severe hot flushes used either an active cooling device (47°F) or a sham device for two weeks, then switched (Uçar et al. *AACE Endoc & Diabetes*. 2025; doi:10.1016/j.aed.2025.09.006).

Results showed the active device reduced severe hot flush episodes by half and total daily hot flushes by a fifth compared to baseline. Benefits were consistent across all groups, and no adverse events occurred.

The findings suggest targeted wrist cooling may provide a safe, non-pharmaceutical option for managing vasomotor symptoms, so this concept may well go forward as the technology matures.

Hypnosis for vasomotor symptoms

Does self-administered hypnosis help reduce vasomotor symptoms? In a trial of 250 postmenopausal women, participants used either hypnosis audio files with cooling imagery and relaxation suggestions or sham white noise auditory material for 6 weeks and their responses evaluated (Elkins et al. *JAMA Netw Open*. 2025; doi:10.1001/jamanetworkopen.2025.42537).

The hypnosis group achieved a 53% reduction in hot flush scores (frequency × severity) compared to 41% in the control group. They also experienced greater decreases in daily interference (49% vs 37%) and more reported perceived benefits (90% vs 64%). These results suggest that self-administered clinical hypnosis effectively reduces hot flush frequency and severity, thus offering an accessible, safe nonhormonal treatment option.

Masturbation for menopausal symptom relief

A survey from the United States investigated masturbation as a menopause symptom management strategy. There were more than 1,000 participants between the ages of 40 and 65 years with nearly one in five perimenopausal and postmenopausal women reporting that self-pleasure provided symptom relief, with one in ten currently using it for symptom management (Lehmiller et al. *Menopause*. 2025; doi:10.1097/GME.0000000000002675).

Masturbation ranked among the highest-rated non-hormonal strategies for vasomotor symptom relief, particularly for psychological symptoms (mood changes) and sleep disturbances. It may also indirectly reduce symptoms such as hot flushes by decreasing stress and improving sleep quality, which can enhance thermoregulation.

Nearly half of respondents indicated openness to trying masturbation if their doctor recommended it. The researchers note that masturbation and partnered sex received the highest ratings for symptom relief compared to other management methods.

The study highlights a significant gap in menopause education among healthcare providers, with up to 90% of US medical trainees feeling unprepared to manage troublesome menopause matters. The authors emphasise that doctors should discuss self-pleasure's potential benefits with patients as part of personalised menopause care. For those who feel coy about opening such a discussion with the word masturbation, using the expression “solo sex” may be an acceptable lead-in ploy.

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