Hormone Therapy: Vasomotor Relief, Bone Health and Risk

Executive Summary for practitioners

REPORT	Menopausal Hormone Therapy—Risks, Benefits and Emerging Options: A Narrative Review
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DESIGN	Narrative review, literature current through September 2025 · emphasis on the last five years

OVERVIEW

This 2025 review synthesizes contemporary evidence on the benefits, risks, and emerging options in menopausal hormone therapy (MHT). It updates the field with route-specific stroke and clot data, current bone health evidence, and estetrol (E4) as a newer treatment option. Central to the review is that benefit and risk both depend on four modifying variables — timing of initiation, route of administration, hormone formulation, and individual baseline risk — rather than on whether MHT is used at all.

KEY FINDINGS

- Hormone therapy reduces hot flash frequency by roughly **70–80% versus baseline**; NAMS estimates a 75% reduction compared with placebo, with relief typically maximal by 8–12 weeks.
- MHT is the **only anti-osteoporotic therapy** with proven efficacy regardless of baseline fracture risk, most effective when started within the first 2–3 years of accelerated postmenopausal bone loss.
- Cardiovascular prevention is **explicitly not an indication** for MHT; major trials including the WHI did not demonstrate protection and raised stroke concerns instead.
- A recent nationwide cohort found transdermal estrogen was not associated with excess ischemic stroke risk, while oral estrogen carried risk consistent with older randomized trials; low-dose vaginal estrogen was associated with lower risk.
- VTE risk varies clearly by formulation: transdermal estradiol lowest, oral estradiol lower than conjugated equine estrogen, ethinyl estradiol highest.
- A 2025 Cochrane meta-analysis found estrogen therapy alone slightly improves overall sexual function, more pronounced when GSM symptoms are treated concurrently.
- Estetrol (E4) shows anti-vasomotor efficacy with favorable pharmacology, but long-term cardiovascular, thrombotic and breast safety data remain pending.

CLINICAL IMPLICATIONS

The clinically actionable framework here is the four-variable model: timing, route, formulation, and baseline risk together determine whether MHT is appropriate for a given patient, rather than a single global answer. For

vasomotor symptom relief in appropriately selected women, particularly within ten years of menopause, the evidence for benefit is strong. For cardiovascular prevention, MHT should not be positioned as protective. Formulation and route decisions — particularly favoring transdermal delivery when thrombotic or cardiometabolic risk factors are present — meaningfully change the safety profile.

PATIENT IMPACT

Much of the public's understanding of hormone therapy risk is still shaped by early-2000s reporting of trials that tested a single oral formulation in an older population. This review supports a more current and more specific conversation: modern data distinguishes risk clearly by route and formulation, transdermal options generally carry a more favorable profile, and newer options like estetrol are entering the picture, though with safety data still accumulating.

IMPLEMENTATION CONSIDERATIONS

- **Clinical:** Document time since menopause and favor initiation within 10 years when appropriate, consistent with the timing/window framework.
- **Clinical:** Favor transdermal estradiol over oral formulations when thrombotic or cardiometabolic risk factors are present.
- **Clinical:** Do not position MHT as cardiovascular prevention; discuss bone protection as a distinct, well-supported indication instead.
- **Communication:** Proactively address early-2000s trial coverage, since it remains the most common source of patient hesitation.

LIMITATIONS & CONTEXT

As a narrative rather than systematic review, study selection reflects editorial judgment, though the authors note deliberate emphasis on literature from the last five years. Long-term safety data for estetrol is explicitly described as pending. Much of the historical risk data, including the WHI, comes from populations that underrepresent racial and ethnic diversity and used a narrower set of formulations than are available today, which may limit how directly those findings generalize to current prescribing practice.

RECOMMENDED NEXT STEPS

1. Review current patients on oral estrogen with thrombotic or cardiometabolic risk factors for a transdermal conversation.
2. Ensure bone health discussions with newly postmenopausal patients happen within the first 2–3 years, when MHT's protective effect is strongest.
3. Separate cardiovascular prevention messaging from hormone therapy counseling entirely.
4. Track estetrol's emerging safety data as it becomes available before broadly recommending it.

RESEARCH SOURCE CITATION

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