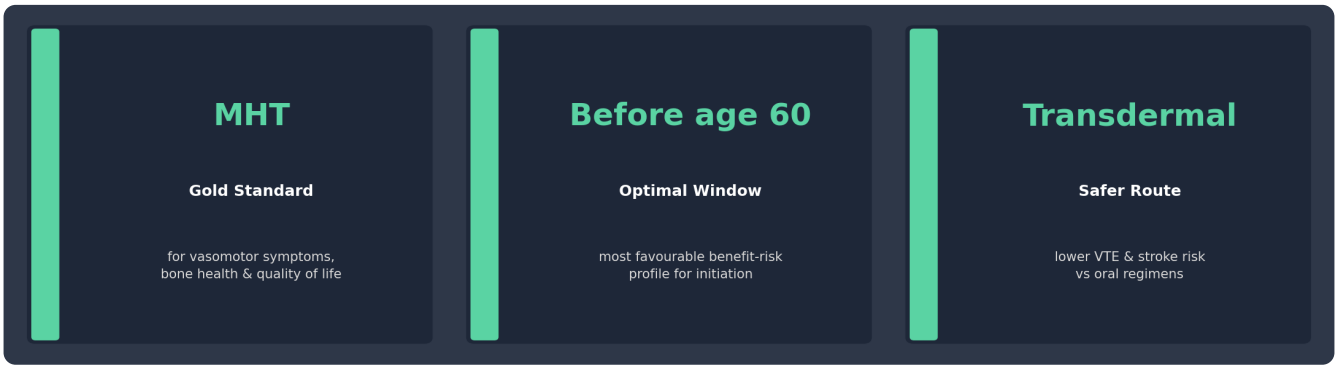
FREE ARTICLE

THE LATEST EVIDENCE ON THE BENEFITS AND RISKS OF MENOPAUSAL HRT

A review of 2025–2026 research on menopausal hormone therapy: efficacy, safety, individualisation, and emerging options



Key evidence highlights from 2025–2026 research [1–3, 10, 12, 14]

Overview

Recent research (2025–2026) confirms that **menopausal hormone therapy (MHT)** remains the most effective treatment for vasomotor symptoms (VMS), genitourinary syndrome of menopause, and prevention of early postmenopausal bone loss, with additional modest improvements in sleep, mood, and quality of life;[1–9] however, the benefit-risk profile is highly dependent on timing, formulation, route of administration, and individual patient factors.

Initiation within 10 years of menopause or before age 60 is associated with a more favourable risk profile, especially when using transdermal estradiol at low to moderate doses.[1,3,10–13] Oral regimens, particularly those using conjugated equine estrogens, are linked to higher risks of venous thromboembolism (VTE) and stroke compared to transdermal options.[1,10,14,15]

Breast cancer risk increases with longer use of combined estrogen-progestogen therapy but is lower with estrogen-only regimens after hysterectomy or when using micronized progesterone.[1,12,16–18] Cardiovascular prevention is not an indication for MHT; risks rise with older age at initiation or pre-existing comorbidities.[6,11,19,20] Newer agents like estetrol (E4) show promise but lack long-term safety data.[1]

KEY PRINCIPLE

Guidelines emphasise individualised therapy, the lowest effective dose, and periodic reassessment. Evidence gaps remain for diverse populations and long-term outcomes.

Authors & journals most frequently cited

TYPE	NAME	PAPERS
Author	O. Ylikorkala	[16] [18]
Author	Heli Siitonen	[18]
Author	Johanna M Joensuu	[16] [18]
Journal	*European Journal of Endocrinology*	[20] [33] [34]
Journal	*Journal of Clinical Medicine*	[17] [35]
Journal	*Climacteric*	[31] [14]

What the research is telling us

Efficacy for symptom relief and bone health

MHT remains the gold standard for alleviating vasomotor symptoms (hot flashes/night sweats), genitourinary syndrome of menopause (GSM), sleep disturbances, mood disorders, and quality of life.[1–8] It also prevents early postmenopausal bone loss and reduces fracture risk in appropriately selected women.[3,7,8,21]

Risks: cardiovascular disease, VTE, and cancer

Risks vary by regimen:

RISK AREA	KEY FINDING	REF.
Cardiovascular disease	No benefit for primary prevention; increased risk if initiated >10 years after menopause or age >60. Transdermal estradiol has lower VTE/stroke risk than oral forms.	[6,11,19,20]
Venous thromboembolism	Higher with oral estrogen plus synthetic progestogens; transdermal routes confer little or no increased risk even in high-risk women.	[10,14]
Breast cancer	Risk increases with duration of combined estrogen-progestogen use; lower with estrogen-only regimens or micronized progesterone/dydrogesterone.	[1,12,16–18]
Endometrial cancer	Unopposed estrogen increases risk; adding progestogen protects the endometrium but may increase breast/VTE risk.	[16,22]
Other cancers	Absolute ovarian cancer risk is small; colorectal cancer evidence is mixed.	[1]

Individualisation: timing, formulation & special populations

Benefits outweigh risks when MHT is started within 10 years of menopause or before age 60 at the lowest effective dose tailored to patient needs.[1–3] Transdermal estradiol with micronized progesterone is preferred for those at higher cardiovascular or VTE risk.[10,12] Special populations, such as women with diabetes or metabolic syndrome, may benefit from transdermal options but require careful screening.[13]

Psychiatric & cognitive outcomes

Evidence for cognitive protection is inconsistent; some studies suggest possible benefit if started early in menopause but no effect, or even increased dementia risk, if started late (>65 years).[17,23,24] Psychiatric adverse events are rare but may be higher in younger women or those receiving systemic rather than local HRT.[25]

In summary

The latest evidence supports MHT as the most effective intervention for menopausal symptom relief and bone health preservation when individualised according to patient characteristics, especially timing since menopause onset and baseline cardiovascular and thrombotic risk factors.[1–3] Transdermal estradiol with micronized progesterone regimens offer improved safety profiles over older oral and synthetic combinations,[10,12] while newer agents like estetrol are promising but require further study.

Risks — including breast cancer (with combined regimens), VTE (especially oral and synthetic progestogens), stroke (older age or initiation more than 10 years post-menopause), and endometrial pathology (unopposed estrogen) — necessitate careful patient selection and ongoing monitoring.[1,11,22] Most guidelines now recommend shared decision-making based on individual preferences and risks rather than blanket recommendations.

Research quality has improved through large cohort studies and meta-analyses, but gaps remain regarding long-term outcomes in diverse populations (e.g., non-white ethnicities), special groups (e.g., breast cancer survivors), psychiatric and cognitive effects beyond symptom relief, and real-world adherence patterns.

While individualised menopausal hormone therapy offers substantial symptomatic relief with acceptable safety for many women when used appropriately, ongoing research is needed to address persistent uncertainties about long-term outcomes across diverse populations and evolving therapeutic options.

Claims & evidence

CLAIM	EVIDENCE STRENGTH	REASONING	PAPERS
MHT is the most effective treatment for vasomotor/ genitourinary symptoms	Strong 10/10	Supported by multiple RCTs/guidelines/meta-analyses across diverse populations	[1–3,5–8]
Early initiation (<10 yrs since menopause) improves benefit-risk ratio	Strong 9/10	Consistent findings across trials/guidelines favouring early use	[1,3,6,11,13]
Transdermal estradiol/micronized progesterone have lower VTE/ breast cancer risk vs oral/synthetic regimens	Strong 8/10	Comparative studies/meta-analyses show reduced adverse events	[10,12,14,16,17]
Combined estrogen-progestogen increases breast cancer risk over time	Strong 8/10	Large cohort/nationwide studies confirm duration-dependent increase	[1,12,16–18]
No cardiovascular prevention benefit; possible harm if started late	Moderate 7/10	RCTs/meta-analyses show neutral/harmful effects if initiated >60 yrs or >10 yrs post-menopause	[6,11,19,20]
Cognitive/psychiatric benefits are uncertain/inconsistent	Moderate 5/10	Mixed results from RCTs/observational studies; some signal for early use	[17,23,24,25]

Research gaps

Matrix showing where research is concentrated versus lacking by topic/outcome and study attribute.

TOPIC / OUTCOME	EARLY INITIATION (<10 YRS)	LATE INITIATION (>10 YRS)	TRANSDERMAL REGIMENS	NON-WHITE POPULATIONS
Vasomotor symptom relief	**18**	2	9	2
Bone health / fracture reduction	**12**	2	6	GAP
Cardiovascular outcomes	**9**	6	5	GAP
Breast / endometrial cancer risk	**11**	4	3	GAP
Cognitive / psychiatric effects	6	2	2	GAP

Future research priorities

Future research should focus on long-term safety and effectiveness in underrepresented groups; regimen-specific risks and benefits; cognitive and psychiatric outcomes; and real-world adherence and persistence patterns.

RESEARCH QUESTION	WHY IT MATTERS
What are the long-term cardiovascular/cancer risks of newer transdermal/bioidentical hormone therapies?	Newer formulations may offer improved safety profiles but lack robust long-term outcome data
How does MHT affect cognitive function/dementia risk when initiated at different ages?	Conflicting evidence exists regarding neuroprotection versus harm depending on timing/formulation
What are optimal strategies for personalising MHT in diverse ethnic/socioeconomic populations?	Most trials underrepresent non-white/minority groups despite differing baseline risks/responses

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