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CLINICIAN NOTE

EVIDENCE SUMMARY

Hormone replacement therapy: who, when and why

Bones before they break · lecture preparation · 15 October 2026, revised 18 October 2026 · For discussion, not a prescription



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Menopausal hormone therapy (MHT, also called HRT) is the most effective treatment for hot flushes and it protects bone. Its risks depend on age, timing, type, route and duration. Guidelines agree it suits symptomatic women under 60 or within 10 years of menopause; they differ on using it for bone alone.

Who it is for

Under 60

THE USUAL INDICATIONS

- Bothersome vasomotor symptoms in women under 60 or within 10 years of menopause. The Menopause Society (NAMS 2022) calls the balance favourable for symptoms and for preventing bone loss[1].
- Premature ovarian insufficiency or early menopause, until at least the average age of natural menopause[2].
- Women at intermediate or high fracture risk within 10 years of menopause, as one first-line option (IMS India)[2].
- Not for preventing heart disease or other chronic disease alone (USPSTF grade D)[3].

CERTAINTY: MODERATE

Benefits

Fractures

WHAT THE TRIALS SHOW

- **Bone.** WHI combined therapy cut hip fractures (HR 0.66) and all fractures (HR 0.76)[4,5]; oestrogen alone cut hip fractures (HR 0.61)[6]. Cochrane 2025 found clinical fractures RR 0.78, moderate certainty[7].
- **Symptoms.** MHT remains the most effective treatment for vasomotor and genitourinary symptoms[1].
- **Deaths.** No change in all-cause, heart or cancer deaths over 18 years of WHI follow-up[8].

Harms

Absolute

PER 10,000 WOMEN PER YEAR (WHI) AND META-ANALYSIS

HARM	SOURCE	SIZE
Breast cancer, combined therapy	WHI[4]	8 extra per 10,000 women per year
Breast cancer, by type and duration	Worldwide meta-analysis[9]	5 years from age 50: about 1 extra case per 50 users (oestrogen + daily progestagen), 1 per 70 (intermittent), 1 per 200 (oestrogen alone)
Breast cancer, oestrogen alone	WHI[6,10]	No increase; cumulative HR 0.79
Stroke	WHI[4,6]	8 extra (combined); 12 extra (oestrogen alone) per 10,000 per year
Venous clots	WHI[4]; UK case-control[11]	8 extra PE per 10,000 per year; oral HRT OR 1.58
Heart disease	WHI[4]; NOGG[12]	7 extra events with combined therapy; no rise when started under 60

Route matters. Oral oestrogen raises clot risk; transdermal oestrogen at standard doses does not, according to the UK guideline[12]. Breast cancer risk rises with duration and is higher with combined than oestrogen-only therapy; little excess follows less than 1 year of use[9].

CERTAINTY: MODERATE

When to start and how long

Window

TIMING

Benefit-risk is better in women under 60 or within 10 years of menopause, and worse after 60 or beyond 10 years because of heart disease, stroke, clots and dementia[1]. WHI women aged 50 to 59 had more favourable results than older women[8,10]. Re-evaluate benefits and risks at intervals, and keep longer use for a documented reason such as persistent symptoms[1].

CERTAINTY: MODERATE *Age-group findings are subgroup analyses.*

What the guidelines say

ESE · NICE · USPSTF · NOGG · NAMS · IMS

GROUP	POSITION ON MHT	ON BONE
ESE 2025, Europe[13]	Covers symptom care, POI and early menopause, and women for whom hormones are not suitable	Treats MHT for chronic disease prevention as a contested question
NICE NG23, UK, updated 2026[14]	Offer HRT for hot flushes and sweats; consider transdermal if clot risk is raised, including BMI over 30	Fracture risk falls while taking HRT; the benefit fades after stopping
NOGG 2024, UK[12]	Option; transdermal avoids extra clot risk	Reduces vertebral, non-vertebral and hip fractures
USPSTF 2022, US[3]	Against for chronic disease prevention (D)	Not a reason on its own
NAMS 2022, US[1]	Favourable under 60 or within 10 years	Prevents bone loss and fracture
IMS International 2024[15]	White paper on prescribing and controversies	Not re-checked in detail
IMS India 2026[2]	Supports MHT in the window	First-line option for intermediate or high risk within 10 years

Gynaecology and orthopaedic literature

WHY THEY SOUND DIFFERENT

Fact. Menopause societies (NAMS, IMS India) list bone protection as a benefit of MHT and, in IMS India, as a first-line bone option near menopause[1,2]. Bone guidelines (NOGG, Endocrine Society, BHOF) are built around fracture risk tools and drugs with fracture trials, with HRT as one option among several[12,16,17]. USPSTF, a prevention body, recommends against MHT for prevention alone[3].

Interpretation (not a sourced finding). The gap reflects the patients each specialty sees. Gynaecologists see younger symptomatic women for whom bone is a bonus. Orthopaedic surgeons see older women after a fracture, where MHT is rarely started and bisphosphonates or denosumab dominate. Both views are consistent with the same trial data.

Practical summary

FOR THE LECTURE

BOTTOM LINE

- Symptomatic woman under 60 or within 10 years of menopause: MHT is reasonable and protects bone[1].
- Early menopause or POI: replace hormones to the average menopause age[2].
- Bone alone, no symptoms: guidelines split; discuss, and consider a bisphosphonate[2,3].
- Prefer transdermal oestrogen when clot risk is raised[12].
- Explain absolute breast cancer numbers by type and duration[9].

WHERE THE EVIDENCE IS WEAK

- WHI used one oral regimen (conjugated equine oestrogen with or without medroxyprogesterone) in women with mean age 63. Modern transdermal oestradiol and micronised progesterone have no comparable fracture or breast cancer RCTs[4,8].
- Only one study in the 2025 Cochrane review focused on perimenopausal women[7].
- Breast cancer figures for type and duration are observational[9].
- The ESE 2025 row is based on the published summary only; the full guideline was not reviewed for this document[13].

References

VERIFIED BY PMID AND DOI, OR PUBLISHER URL · VANCOUVER STYLE

1. “The 2022 Hormone Therapy Position Statement of The North American Menopause Society” Advisory Panel. The 2022 hormone therapy position statement of The North American Menopause Society. Menopause. 2022. PMID 35797481; doi:10.1097/GME.0000000000002028
2. Meeta M, Anuradha M, Ashraf AB, et al. Clinical Practice Guidelines for Menopause: An Executive Summary and Recommendations: Indian Menopause Society 2026. J Midlife Health. 2026. PMID 41767293; doi:10.4103/jmh.jmh_302_25
3. US Preventive Services Task Force, Mangione CM, Barry MJ, et al. Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Persons: US Preventive Services Task Force Recommendation Statement. JAMA. 2022. PMID 36318127; doi:10.1001/jama.2022.18625
4. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. JAMA. 2002. PMID 12117397; doi:10.1001/jama.288.3.321
5. Cauley JA, Robbins J, Chen Z, et al. Effects of estrogen plus progestin on risk of fracture and bone mineral density: the Women's Health Initiative randomized trial. JAMA. 2003. PMID 14519707; doi:10.1001/jama.290.13.1729
6. Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. JAMA. 2004. PMID 15082697; doi:10.1001/jama.291.14.1701
7. Bofill Rodriguez M, Yong LN, Mirkov S, et al. Long-term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev. 2025. PMID 41307293; doi:10.1002/14651858.CD004143.pub6
8. Manson JE, Aragaki AK, Rossouw JE, et al. Menopausal Hormone Therapy and Long-term All-Cause and Cause-Specific Mortality: The Women's Health Initiative Randomized Trials. JAMA. 2017. PMID 28898378; doi:10.1001/jama.2017.11217
9. Collaborative Group on Hormonal Factors in Breast Cancer. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. Lancet. 2019. PMID 31474332; doi:10.1016/S0140-6736(19)31709-X
10. Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. JAMA. 2013. PMID 24084921; doi:10.1001/jama.2013.278040
11. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases. BMJ. 2019. PMID 30626577; doi:10.1136/bmj.k4810
12. Gregson CL, Armstrong DJ, Avgerinou C, et al. The 2024 UK clinical guideline for the prevention and treatment of osteoporosis. Arch Osteoporos. 2025. PMID 40921943; doi:10.1007/s11657-025-01588-3
13. Lumsden MA, Dekkers OM, Faubion SS, et al. European society of endocrinology clinical practice guideline for evaluation and management of menopause and the perimenopause. Eur J Endocrinol. 2025. PMID 41082911; doi:10.1093/ejendo/lvaf206
14. National Institute for Health and Care Excellence. Menopause: identification and management. NICE guideline NG23. Published 12 November 2015, last updated 15 April 2026. https://www.nice.org.uk/guidance/ng23
15. Panay N, Ang SB, Cheshire R, et al. Menopause and MHT in 2024: addressing the key controversies - an International Menopause Society White Paper. Climacteric. 2024. PMID 39268862; doi:10.1080/13697137.2024.2394950
16. Eastell R, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society* Clinical Practice Guideline. J Clin Endocrinol Metab. 2019. PMID 30907953; doi:10.1210/jc.2019-00221
17. LeBoff MS, Greenspan SL, Insogna KL, et al. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022. PMID 35478046; doi:10.1007/s00198-021-05900-y