Menopausal Hormone Therapy in Perimenopause and Menopause: Indications, Benefits, Risks, and Individualized Care

Abstract

Menopausal hormone therapy remains an effective option for bothersome symptoms, yet prescribing continues to be influenced by polarized interpretations of its benefits and risks. This critical narrative review examines its role during perimenopause and after menopause, integrating pivotal randomized trials, observational studies, systematic reviews, and recent recommendations. Systemic therapy is the most effective treatment for vasomotor symptoms and prevents bone loss and fractures during use. In symptomatic women without contraindications, initiation before age 60 or within 10 years of menopause generally provides a more favorable benefit-risk context than later initiation. This timing does not guarantee individual safety or establish an indication for cardiovascular prevention. Risks vary with baseline health, estrogen formulation, route, progestogen exposure, and treatment duration. Evidence suggesting a lower venous thromboembolic risk with transdermal rather than oral estrogen is predominantly observational; comparative breast safety data for different progestogens are similarly limited. Improvements in sleep or metabolic markers should not be converted into independent indications for weight management or diabetes prevention. Perimenopause requires a separate assessment of contraception, abnormal bleeding, and endometrial protection. Local treatment is usually more proportionate for isolated genitourinary symptoms. Recent European, international, North American, and British recommendations agree on shared decision-making but differ in some interpretations and contraindication pathways. Regulatory changes and newer nonhormonal treatments must be interpreted within their jurisdictions. Appropriate prescribing therefore requires a defined clinical objective, transparent discussion of absolute and relative risks, individualized treatment selection, and periodic reassessment, including recognition that choosing no systemic therapy can be appropriate.

Keywords: menopausal hormone therapy; perimenopause; menopause; vasomotor symptoms; venous thromboembolism; breast cancer; individualized care.

Introduction

Menopausal hormone therapy (MHT) has established symptomatic efficacy, but its clinical use remains shaped by controversies over chronic disease prevention. The European Society of Endocrinology (ESE) guideline emphasizes a patient-centered approach that considers symptoms, comorbidities, and preferences [1]. The 2022 North American Menopause Society (NAMS) position statement distinguishes treatment of menopausal symptoms from population-wide preventive prescribing [2]. The International Menopause Society (IMS) recommendations published in late 2025 broaden the discussion to midlife health and should be read with their 2026 correction [3,4]. These documents do not make all formulations interchangeable or resolve every uncertainty concerning long-term exposure.

The clinically relevant question is which intervention may benefit a particular woman, for which indication, and with what uncertainty. Randomized treatment effects, observational associations, and recommendations that integrate several evidence streams must remain distinct. This review critically examines the benefits and risks of MHT during perimenopause and after menopause, with particular attention to cardiometabolic comorbidity, endometrial protection, and shared decision-making. Its purpose is to support proportionate treatment rather than universal hormone replacement.

Review

Literature search and selection

This targeted narrative review builds on a literature search conducted on October 26, 2026, with a documented PubMed verification and search update on October 27, 2026. PubMed records were accessed through public pages and National Library of Medicine E-utilities. Public Cochrane summaries and relevant society and regulatory documents were consulted. No institutional Scopus, Web of Science, or separate Ovid MEDLINE search was performed. The principal terms covered menopause, perimenopause, hormone therapy, vasomotor symptoms, breast cancer, venous thromboembolism, cardiovascular disease, progesterone, transdermal estradiol, sleep, and insulin resistance. The reproducible update queries, dates, retrieval limits, and selection rationale are provided in Appendix A.

Priority was given to guidelines, systematic reviews, pivotal randomized trials, large observational studies informing contemporary formulations, and human experimental studies relevant to metabolic interpretation. English-language publications were assessed, and French-language clinical material was considered where accessible. Selection was purposive rather than exhaustive and favored

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studies that distinguished the intervention, population, outcome, and follow-up period. Reference metadata were checked against PubMed records. Full texts were consulted when accessible; other assessments relied on abstracts or official summaries. There was no duplicate screening, registered protocol, formal study-level risk-of-bias assessment, or original meta-analysis. The review is therefore not presented as systematic. Historical search procedures that were not fully logged cannot be reconstructed retrospectively. Lack of access to every full text and selective retrieval remain limitations.

Defining the menopausal transition

Natural menopause is recognized retrospectively after 12 months of amenorrhea without another cause. Perimenopause encompasses fluctuating ovarian function, cycle changes, and symptoms that may precede the final menstrual period. The Stages of Reproductive Aging Workshop framework (STRAW+10) describes this progression without reducing reproductive aging to an isolated hormone measurement [5]. The Study of Women's Health Across the Nation (SWAN) demonstrates substantial variability and potentially prolonged vasomotor symptoms, precluding reassurance that symptoms invariably resolve quickly [6].

In women older than 45 with a typical presentation, diagnosis is usually clinical. Biochemical assessment may be useful between 40 and 45 when uncertainty persists; suspected premature ovarian insufficiency (POI) before age 40 requires a distinct evaluation. Updated POI guidance uses menstrual disturbance for at least four months and follicle-stimulating hormone (FSH) above 25 IU/L, with repeat testing after four to six weeks when uncertainty remains [7]. These criteria should not be applied indiscriminately during hormone use. NICE advises against using FSH to identify menopause during combined estrogen-progestogen contraception or high-dose progestogen use. After hysterectomy, menstrual staging is unavailable, and age, symptoms, treatment exposure, and clinical context guide assessment [8]. Pregnancy, thyroid disease, anemia, depression, sleep apnea, and gynecologic pathology must not be overlooked by attributing every symptom to menopause.

Interpreting the Women's Health Initiative

The 2002 Women's Health Initiative (WHI) report challenged cardiovascular benefits previously inferred largely from observational studies. It randomized 16,608 women with a uterus to oral conjugated equine estrogens (CEE), 0.625 mg/day, plus medroxyprogesterone acetate (MPA), 2.5 mg/day, or placebo. Early stopping reflected an unfavorable global balance, including breast and vascular outcomes [9]. These findings concern a specified regimen in women aged 50-79; they neither directly evaluate every contemporary formulation nor justify dismissing randomized evidence because prescribing has changed.

The integrated analysis of both WHI hormone trials, including CEE alone after hysterectomy, demonstrates different outcome profiles by regimen and age and does not support general chronic disease prevention [10]. At 18 years of follow-up, overall mortality did not differ significantly between randomized treatment groups. This does not establish a universal longevity benefit or negate specific adverse outcomes [11]. The September 2026 Cochrane review included 24 studies and 45,660 participants, but its search ended on September 26, 2024, and much of its evidence remained dependent on older oral regimens [12]. Publication recency must therefore be distinguished from recency of the underlying trials.

Established benefits and measurable treatment goals

Bothersome vasomotor symptoms are the principal indication for systemic MHT after natural menopause. Randomized comparisons establish efficacy for reducing symptom frequency and severity, including the historical Cochrane synthesis of oral therapy [13]. Treatment success should be defined with the patient in terms of functioning, sleep disruption, or symptom burden, rather than a target serum estradiol concentration. Symptom improvement is a valid therapeutic outcome even when prevention of future disease has not been demonstrated.

For isolated genitourinary syndrome of menopause, systemic exposure may be unnecessary. Low-dose vaginal estrogen can improve atrophic symptoms, although comparative efficacy and prolonged safety estimates are less certain [14]. A local treatment can also supplement systemic therapy when vulvovaginal symptoms persist. Persistent pain or urinary symptoms require assessment for competing diagnoses. Treatment choice should reflect the symptom target, not an assumption that every manifestation requires systemic estrogen.

MHT prevents bone loss and reduces fractures while used. The cited 2026 Cochrane review estimated a relative risk of clinical fracture of 0.78 (95% confidence interval (CI), 0.71-0.86) for the combined regimen studied [12]. This is not proof that MHT is preferable to osteoporosis-specific agents for every woman with established osteoporosis. Age, fracture probability, symptoms, alternatives, and the management plan after withdrawal remain relevant. The ESE suggestion to consider initiation for bone protection in selected asymptomatic women younger than 60 is conditional and should not become a universal prescribing rule [1].

Sleep, body composition, and glucose metabolism

Sleep complaints are multifactorial. The meta-analysis by Cintron and colleagues found improved subjective sleep quality primarily in women with baseline vasomotor symptoms, rather than a consistent benefit across all menopausal populations [15]. Trials of micronized progesterone suggest improvements in some sleep outcomes, but small samples, variable measures, and concomitant estradiol limit interpretation [16]. Persistent insomnia, obstructive sleep apnea, and restless legs require their own diagnostic and therapeutic pathways.

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A crossover experiment involving 38 women, including 11 postmenopausal participants, found increased homeostatic model assessment of insulin resistance (HOMA-IR) after six weeks of moderate sleep restriction without demonstrated mediation by adiposity. It did not test MHT and cannot establish that hormone-mediated sleep improvement prevents diabetes [17]. SWAN associates the transition with accelerated fat gain and lean mass loss, without necessarily accelerating overall weight gain [18]. Estrogen-related hepatic, muscle, adipose, and beta-cell mechanisms are biologically plausible, but part of the mechanistic evidence is preclinical and should not be treated as proof of clinical prevention [19].

The older Salpeter meta-analysis reported favorable HOMA-IR changes and lower incident diabetes, with a relative risk of 0.7 (95% CI, 0.6-0.9) in women without diabetes [20]. Formulations, study methods, and outcome definitions varied. Fasting indices do not provide the same information as a clamp, and HOMA-IR has no universal clinical threshold. Reduced insulin resistance, lower glucose, and fewer diabetes diagnoses are related but noninterchangeable outcomes. These findings do not create an independent indication for MHT as an antidiabetic or weight-loss treatment.

Timing and cardiovascular outcomes

Timing modifies baseline vascular risk and the biological context of treatment. The Early versus Late Intervention Trial with Estradiol (ELITE) randomized 643 women after stratification by time since menopause. Oral estradiol slowed carotid intima-media thickness progression in the early stratum but not the late stratum. This intermediate outcome does not demonstrate fewer myocardial infarctions [21]. The Kronos Early Estrogen Prevention Study (KEEPS) did not show significantly slower carotid progression in recently menopausal women and lacked power to determine major clinical event differences [22]. Neither trial validates carotid imaging as an individual prediction of cardiovascular benefit from MHT.

The cardiovascular Cochrane review reported more favorable subgroup estimates with initiation within 10 years, alongside increased venous thromboembolic risk; these exploratory comparisons do not establish a general preventive indication [23]. ESE recommends against MHT primarily for cardiovascular primary or secondary prevention, whereas IMS gives greater weight to possible coronary and mortality benefits in healthy women starting early and describes use solely for coronary prevention as off-label [1,3]. This is a difference in interpretation, not complete consensus. On February 12, 2026, the US Food and Drug Administration (FDA) announced labeling changes for six hormone therapy products [24]. Regulatory reassessment is not a new comparative trial and cannot automatically define authorization or practice in another jurisdiction.

Venous thromboembolism and route of administration

Oral estrogen first-pass hepatic exposure influences hemostatic pathways. In the observational QResearch/CPRD study, the adjusted odds ratio for venous thromboembolism was 1.58 (95% CI, 1.52-1.64) with oral treatment and 0.93 (95% CI, 0.87-1.01) with transdermal treatment, each compared with nonuse [25]. ESTHER also found associations differing by route and progestogen [26]. Confounding by indication, dose selection, patient characteristics, and imperfect exposure classification remain possible. Absence of a statistically significant association is not proof of zero risk.

Transdermal estrogen is often preferred when vascular or metabolic concerns influence prescribing, but the evidence is compatible with a lower risk rather than a randomized guarantee of safety. Observational stroke findings also vary by dose and route [27]. A history of thrombosis remains a specialist situation. ESE allows consideration of low-dose transdermal estrogen after individualized assessment if an indication persists, while the NAMS systemic-therapy contraindication framework is more restrictive [1,2]. Changing route does not erase a contraindication, and high-risk situations should not be managed by a simplified route-selection rule.

Breast outcomes and progestogen selection

The 2020 WHI breast follow-up found higher incidence after randomized CEE-MPA than placebo, hazard ratio (HR) 1.28 (95% CI, 1.13-1.45), and lower incidence after CEE alone in hysterectomized women, HR 0.78 (95% CI, 0.65-0.93) [28]. The populations were different and were not randomized directly between these regimens. Prolonged follow-up also does not represent continuous treatment throughout observation. These findings do not justify estrogen for breast cancer prevention.

The international observational meta-analysis linked breast risk to treatment type and duration [29]. In E3N, relative risks were 1.00 (95% CI, 0.83-1.22) for estrogen-progesterone, 1.16 (95% CI, 0.94-1.43) for estrogen-dydrogesterone, and 1.69 (95% CI, 1.50-1.91) for estrogen with other progestogens [30]. The latter category is heterogeneous and should not be equated with all synthetic progestogens. British observational data also suggest variability by molecule and duration [31]. Micronized progesterone may be considered in this context, but long-term comparative randomized breast safety is unproven. Transdermal delivery does not guarantee superior breast safety. Systemic MHT is generally avoided after breast cancer, with exceptional circumstances requiring multidisciplinary assessment [1,2].

Communicating absolute and relative risks

A relative estimate must be discussed alongside the comparator, outcome, duration, and baseline population. In the initial WHI combined-treatment report, the published absolute excesses were eight invasive breast cancers, eight strokes, and eight pulmonary emboli per 10,000 person-years, with five fewer hip fractures per 10,000 person-years [9]. These are event-specific estimates from

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that trial, not predictions for a younger woman using transdermal estradiol and micronized progesterone. They must not be added without accounting for overlap or projected linearly over an arbitrary duration.

In the 2020 WHI breast analysis, the reported annualized incidence was 0.45% versus 0.36% for CEE-MPA and its placebo group, and 0.30% versus 0.37% for CEE alone and its separate placebo group [28]. These observed rates derive from a different follow-up analysis than the 2002 report and should not be presented as five-year cumulative risks. Both absolute and relative estimates carry uncertainty. Personalized discussion should acknowledge when a formulation-specific absolute estimate is unavailable rather than import a precise number from another regimen.

Endometrial protection and bleeding

Systemic estrogen requires adequate progestogen protection when the uterus is present. The 2025 Cochrane review supports the importance of avoiding unopposed estrogen but does not establish one minimum progestogen dose for every estrogen regimen; endometrial cancer events were too uncommon for definitive comparisons [32]. Protection depends on estrogen exposure, progestogen, schedule, and adherence. Common oral micronized progesterone schedules of 200 mg for 12-14 days monthly or 100 mg continuously are clinical reference regimens, not universal doses independent of estrogen exposure [1,33].

Heavy, prolonged, late-onset, or risk-associated bleeding should not be dismissed as treatment adaptation. Investigation depends on the treatment timeline, examination, and endometrial risk; a six-month adjustment period is not appropriate in every case. The British Menopause Society (BMS) pathway and the April 2026 NICE update provide relevant frameworks [8,33]. Low-dose vaginal estrogen usually does not require routine progestogen addition, but persistent or postmenopausal bleeding still warrants evaluation. Estrogen alone is usual after hysterectomy, although residual endometriosis may alter the approach [1,2].

Perimenopause, contraception, and comorbidity

MHT is not contraception. A 52 mg levonorgestrel intrauterine device may provide contraception and endometrial protection alongside estrogen prescribed for symptoms. The Faculty of Sexual and Reproductive Healthcare (FSRH) supports five years of use for endometrial protection; longer contraceptive durations for some devices must not be extrapolated to this indication, and local licensing requires verification [34]. Sequential therapy may suit the transition, with counseling about expected withdrawal bleeding and investigation of abnormal patterns.

Well-controlled diabetes and controlled hypertension do not independently preclude MHT. ESE favors transdermal estrogen in these settings and advises against starting MHT during uncontrolled hypertension. Migraine with aura requires vascular assessment and favors a transdermal approach when MHT is indicated; menopausal therapy should not be equated with combined contraceptive estrogen exposure [1]. Prior coronary disease, stroke, thrombosis, active liver disease, or unexplained bleeding requires a different pathway and often specialist advice. In POI, hormone replacement until the usual age of menopause is generally recommended without contraindications even when vasomotor symptoms are absent, while fertility, etiology, bone health, and psychological support remain relevant [7].

Nonhormonal alternatives and newer treatments

NAMS supports selected selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, gabapentin, cognitive behavioral therapy, and fezolinetant for appropriate patients with vasomotor symptoms [35]. Benefits, interactions, adverse effects, preference, and access determine selection. Lifestyle measures support health but should not be described as equivalent to MHT for reducing hot-flash frequency.

SKYLIGHT 1 demonstrated symptomatic efficacy of the neurokinin-3 antagonist fezolinetant [36]. US safety guidance requires hepatic assessment before treatment, monthly during the first three months, and at months six and nine [37]. Elinzanetant, a neurokinin-1/3 antagonist, reduced vasomotor symptoms and improved sleep scores in OASIS 1 and 2 [38]. Its US prescribing information includes daytime impairment or somnolence, hepatic assessment initially and at three months, cytochrome P450 3A4 (CYP3A4) interactions, and seizure precautions [39]. These are jurisdiction-specific requirements; current local labeling takes precedence. Neither agent has established fracture, cardiovascular, or diabetes-prevention benefits. Cognitive behavioral therapy for insomnia can improve persistent insomnia, as demonstrated in MsFLASH, without establishing diabetes prevention [40].

Applicability to care in Morocco

International recommendations inform clinical reasoning but do not establish Moroccan marketing authorization, availability, reimbursement, or cost. This review did not verify a current national product register, prices, or a comprehensive Moroccan MHT guideline. Before prescribing, clinicians should confirm authorization and the locally applicable product information, formulation and dose availability, affordability, and access to required monitoring. A US label should not be used to imply Moroccan approval of fezolinetant or elinzanetant.

Practical treatment planning should also establish access to gynecologic assessment, ultrasound or endometrial sampling when indicated, and breast, vascular, or menopause expertise for complex cases. These are implementation requirements, not claims that a uniform referral network or organized screening program exists nationally. A theoretically favorable prescription may be

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inappropriate when safe monitoring or essential investigation cannot be arranged. Such constraints should be discussed explicitly rather than treated as patient nonadherence.

Shared decisions and follow-up

Initial assessment establishes the indication, reproductive stage, uterus status, bleeding, contraceptive needs, history, blood pressure, and breast and vascular risk. Testing is directed by clinical findings and usual screening rather than routine extensive hormonal or thrombophilia panels. Regulated estradiol and micronized progesterone must be distinguished from compounded products marketed as bioidentical, for which superior safety is unproven [2]. ESE recommends reassessing treatment effects at three months; inadequate benefit prompts review of the diagnosis, dose, formulation, or route. Continued use requires a persisting favorable balance and periodic, generally annual, reassessment [1].

There is no universal requirement to stop at five years or age 65. Continuation and late initiation are different decisions; increasing age and exposure still warrant renewed discussion. Choosing no systemic MHT is a valid individualized outcome. The indications and limitations of evidence are summarized in Table 1.

Clinical target	Type of evidence	Supported finding	Clinical limitation
Bothersome vasomotor symptoms	Randomized trials and systematic review	MHT reduces symptoms [13].	Assess patient-important benefit and contraindications.
Isolated genitourinary symptoms	Randomized trials; systematic review	Local estrogen improves atrophic symptoms [14].	Comparative and prolonged safety evidence is limited.
Bone health	Randomized trials; systematic review	Fracture reduction with the regimens studied [12].	Compare with osteoporosis-specific treatment and plan reassessment after stopping.
Sleep	Systematic review of trials	Benefit mainly with concomitant vasomotor symptoms [15].	Does not treat every cause of insomnia or apnea.
Insulin resistance and incident diabetes	Older randomized trial meta-analysis	Some favorable metabolic outcomes [20].	No independent indication for diabetes prevention or weight management.
Cardiovascular prevention	Randomized trial meta-analysis; subgroup analyses	No established overall preventive indication [23].	Timing subgroups do not justify universal prevention.
POI	Clinical guideline integrating limited direct evidence	Replacement generally recommended until usual menopause age [7].	Different clinical setting from later initiation; assess contraindications and fertility.

Table 1: Clinical indications for menopausal hormone therapy: evidence and limitations

MHT: menopausal hormone therapy; POI: premature ovarian insufficiency. Supporting references are provided in the table.

The pivotal studies answer different questions and should not be treated as interchangeable evidence of contemporary formulation safety. Their designs and principal limitations are compared in Table 2.

Study and population	Design and treatment	Main finding	Important limitation
WHI 2002; 16,608 women with a uterus [9]	Randomized; CEE 0.625 mg/day + MPA 2.5 mg/day versus placebo	Unfavorable global balance; vascular and breast signals.	Specified oral regimen and population; no direct evaluation of current transdermal combinations.
WHI integrated analysis; 27,347 women [10]	Two separate randomized trials according to hysterectomy status	Different profiles by regimen and age.	No direct randomization between the two regimens.
WHI breast follow-up [28]	Follow-up after randomized exposure	HR 1.28 for CEE-MPA; HR 0.78 for CEE alone versus respective placebo.	Different populations; extended follow-up is not continuous exposure.
ELITE; 643 women [21]	Randomized estradiol; timing strata	Less carotid progression in early stratum.	Intermediate outcome; no demonstrated infarction reduction.
KEEPS [22]	Randomized oral CEE or transdermal estradiol with cyclic progesterone versus placebo	No significant slowing of carotid progression.	Insufficient power for major clinical events.
E3N; 80,377 women [30]	Observational cohort	Associations differed by progestogen.	Residual confounding; heterogeneous exposure groups.
QResearch/CPRD; 80,396 cases and 391,494 controls [25]	Nested case-control study	Oral OR 1.58; transdermal OR 0.93 versus nonuse.	No randomized proof of equivalence or zero risk.
Sleep restriction; 38 women, 11 postmenopausal [17]	Randomized crossover experiment; six weeks	Higher HOMA-IR without demonstrated adiposity	Small subgroup; MHT was not tested.

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		mediation.	
OASIS 1 and 2 [38]	Randomized elinzanetant 120 mg versus placebo; controlled phase 12 weeks	Vasomotor and sleep score improvements.	No established chronic disease prevention.

Table 2: Selected pivotal studies informing menopausal care: designs, findings, and limitations

WHI: Women's Health Initiative; CEE: conjugated equine estrogens; MPA: medroxyprogesterone acetate; HR: hazard ratio; OR: odds ratio; CI: confidence interval; HOMA-IR: homeostatic model assessment of insulin resistance; CPRD: Clinical Practice Research Datalink. Supporting references are provided in the table.

Clinical options should be considered according to the indication, contraindications, and feasible monitoring rather than ranked as universally safest. Table 3 summarizes these choices.

Option	When it may be considered	Main precautions
Systemic estrogen with appropriate progestogen when needed	Bothersome symptoms requiring systemic treatment [1].	Uterus status, baseline risk, dose, route, and reassessment.
Transdermal estradiol	When route selection is influenced by vascular or metabolic concerns [1,25].	Observational evidence compatible with lower venous risk; does not remove contraindications.
Micronized progesterone	Endometrial protection with an appropriate estrogen dose and schedule [1,33].	Adherence and adequate exposure; no guarantee of breast safety.
52 mg levonorgestrel intrauterine device with estrogen if indicated	Perimenopausal contraceptive and endometrial protection needs [34].	Five years for endometrial protection under FSRH guidance; confirm local authorization.
Low-dose vaginal estrogen	Isolated genitourinary symptoms [14].	After breast cancer, consider only after nonhormonal failure and specialist discussion [1].
Selected SSRIs/SNRIs or gabapentin	When nonhormonal vasomotor treatment fits preference or contraindications [35].	Interactions and adverse effects; no established bone benefit.
Fezolinetant	Vasomotor symptoms when an authorized and accessible option [36].	Local authorization and availability unverified; hepatic precautions and locally applicable monitoring [37].
Elinzanetant	Vasomotor symptoms when authorized and accessible [38].	Local authorization and availability unverified; somnolence, CYP3A4 interactions, liver monitoring, seizure precautions [39].
Cognitive behavioral therapy for insomnia	Persistent insomnia during the transition [40].	Sleep benefit does not establish diabetes prevention.

Table 3: Therapeutic options for menopausal symptoms: individualized selection and precautions

Treatment selection requires individualized assessment of symptoms, contraindications, baseline risks, patient preferences, and local availability. Supporting references are provided in the table.

Guidelines and regulatory documents differ in purpose, population, evidentiary framework, and jurisdiction. Table 4 identifies agreement and relevant distinctions rather than implying uniform recommendations.

Source and jurisdiction	Population and scope	Agreement relevant to care	Differences or uncertainty
ESE 2025; European professional guideline [1]	Perimenopause, menopause, and POI; evaluation and management	Individualized indication, uterine protection, early reassessment.	Selected prior-VTE situations may be considered for low-dose transdermal therapy after individual assessment; no primary cardiovascular-prevention indication.
NAMS 2022/2023; North American position statements [2,35]	Hormonal treatment and nonhormonal vasomotor options	Symptom-directed shared decisions and periodic review.	More restrictive systemic-MHT contraindication framework for prior VTE; not a local product authorization.
IMS 2025 with 2026 correction; international guidance [3,4]	Broad midlife health and menopause care	Individualization and separation of symptom treatment from other care.	Greater emphasis on possible early-initiation coronary benefits; prevention-only prescribing described as off-label.
NICE NG23; England [8]	Diagnosis and management; updated bleeding advice	Clinical diagnosis in typical settings; informed treatment choice.	Jurisdiction-specific referral pathways; do not apply FSH indiscriminately during hormonal contraception.
BMS joint guidance; UK [33]	Unscheduled bleeding on MHT	Adequate progestogen and assessment of concerning	Investigation depends on timing, bleeding pattern, and

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		bleeding.	endometrial risk.
FSRH; UK [34]	Contraception in women older than 40	MHT is not contraception; integrate contraceptive needs.	Five-year endometrial protection recommendation is distinct from contraceptive device duration and local licensing.
FDA and US labels [24,37,39]	Product-specific authorization, warnings, and monitoring	Attention to indication and adverse effects.	Regulatory decisions are not clinical trials and do not establish Moroccan authorization or availability.

Table 4: Comparison of major menopause recommendations: areas of agreement, differences, and jurisdiction

ESE: European Society of Endocrinology; NAMS: North American Menopause Society; IMS: International Menopause Society; NICE: National Institute for Health and Care Excellence; BMS: British Menopause Society; FDA: Food and Drug Administration; POI: premature ovarian insufficiency; MHT: menopausal hormone therapy. Recommendations and regulatory decisions should be interpreted within their respective populations and jurisdictions. Supporting references are provided in the table.

Limitations and research priorities

Evidence does not cover every contemporary combination, dose, route, or duration. Large observational datasets remain valuable for rare outcomes but are vulnerable to selection, exposure changes, and residual confounding. Age and timing subgroup analyses may be exploratory, and intermediate vascular markers cannot substitute for demonstrated clinical benefit. POI, perimenopause, women with multiple comorbidities, and populations underrepresented in pivotal trials require additional study. Priorities include comparative long-term safety of contemporary regimens, patient-important outcomes, and implementation under differing resource constraints. Selective retrieval and incomplete full-text access additionally limit this narrative synthesis.

Conclusions

MHT should be considered when a defined clinical indication is matched to an acceptable individual benefit-risk profile. Its symptomatic efficacy deserves recognition, while uncertainty concerning particular formulations and prolonged exposure should remain explicit. Individualization begins with deciding whether systemic treatment is needed, then extends to route, dose, endometrial protection, and follow-up. Shared decisions should communicate risk in understandable terms, preserve access to effective alternatives, and recognize that declining MHT can be appropriate. This approach supports useful treatment without turning menopause into a universal indication for medication.

Declarations

Ethics approval: Ethics committee approval was not required for this narrative review, which is based on previously published literature and does not involve new patient-level data.

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