ROPER ST. FRANCIS HEALTHCARE

Perimenopause and Hormone Therapy

Evidence-based management for Primary care

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02/07/2026

DISCLOSURE/BIAS

Disclosure Statement

Planners, faculty, and authors have disclosed no relevant financial relationships with ineligible companies related to the content of this activity.

Content Validation Statement

This activity is based on current evidence and clinical guidelines. Generic names are used where possible. Treatment recommendations reflect accepted standards of care.

CME NEEDS ASSESSMENT

Educational Gap:

Perimenopause and menopausal hormone therapy are frequently underdiagnosed or undertreated in primary care due to outdated safety concerns, confusion about estrogen formulations, and overreliance on laboratory testing rather than symptom-based diagnosis.

Practice Gap:

Primary care clinicians report uncertainty regarding:

- Safe estrogen routes and formulations
- Appropriate use of progesterone
- Management of perimenopausal symptoms prior to menopause

Desired Outcome:

Improve clinician confidence in prescribing evidence-based, risk-stratified hormone therapy to improve patient quality of life.

LEARNING OBJECTIVES

At the conclusion of this activity, participants will be able to:

1. Identify common perimenopausal symptoms appropriate for hormone therapy in primary Care.

2. Compare estrogen formulations and routes of administration based on cardiovascular and thrombotic risk.

3. Apply symptom-driven, individualized hormone therapy strategies consistent with current guidelines.

4. Counsel patients effectively regarding benefits, risks, and misconceptions of hormone therapy.

What is Perimenopause?

And what is happening in the body?

Perimenopause

- Transitional phase preceding menopause
  - Menopause confirmed after 12 months of amenorrhea
- Median onset: age 47; typical duration 4–10 years

Pathophysiology

- Ovarian signaling instability: Decline and fluctuation in ovarian follicular activity
- Hormonal variability, not estrogen deficiency
  - Estrogen levels vary widely—can be supraphysiologic
- Progressive decline in inhibin B → ↑ FSH levels
- Neuroendocrine instability
  - Contributes to vasomotor symptoms
  - Neurologic symptoms common

What is Perimenopause?

Clinical Presentation

- Vasomotor symptoms (hot flashes, night sweats)
- Menstrual irregularity (shorter cycles, skipped cycles)
- Sleep disruption, anxiety, mood changes
- Genitourinary syndrome: vaginal dryness, dyspareunia, recurrent UTIs
- Cognitive complaints (fatigue, "brain fog")

Diagnosis in Primary Care

- Clinical diagnosis based on symptoms and menstrual changes
- Rule out pregnancy, thyroid disease, and anemia when indicated
- Consider evaluating for abnormal uterine bleeding etiologies
- FSH testing not routinely recommended due to variability

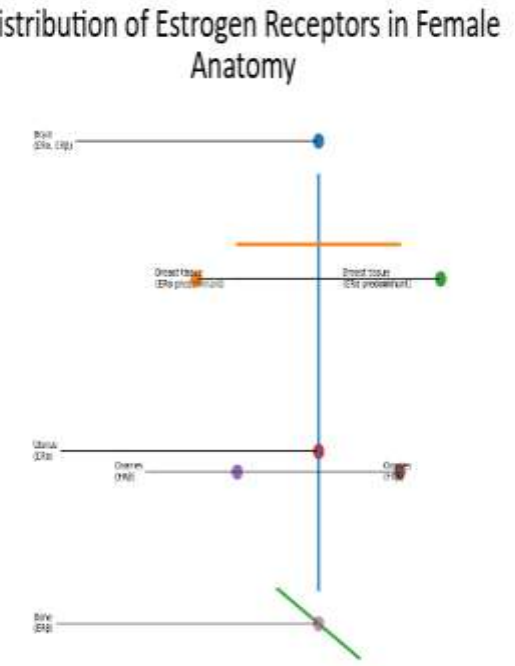

Figure. Major estrogen receptor (ERα and ERβ) distribution in female tissues.

Management Strategies

Lifestyle Modifications

- Exercise
- Weight management
- Sleep hygiene
- Limiting alcohol consumption

Over the Counter

- Supplements: Black Cohosh, Ashwagandha, Berberine, Inositol
- Vaginal moisturizers

Non-Hormonal prescriptions

- SSRIs/SNRIs
- Gabapentin
- fezolinetant

Hormonal

- Localized: vaginal estrogen, prasterone, DHEA
- Systemic HRT
- Birth control: OCPs, IUDs, vaginal ring

Hormonal Management

HRT Pros and Cons

Pros:

- **Estrogen**
  - Most effective treatment for vasomotor symptoms
  - Improves genitourinary syndrome of menopause (GSM)
  - Prevents bone loss and reduces fracture risk
- **Progesterone**
  - Protects endometrium when estrogen is used
  - May improve sleep quality
  - Option for bleeding control in select patients
- **Combined Estrogen–Progestogen Therapy**
  - Effective relief of vasomotor symptoms
  - Endometrial protection in patients with uterus
  - Multiple regimens allow individualized therapy

Cons:

- **Estrogen**
  - Requires progestogen if uterus present
  - Risk of VTE, stroke varies by route, dose, timing
  - Not appropriate in estrogen-dependent malignancy
- **Progesterone**
  - Does not treat vasomotor symptoms alone
  - Mood changes, bloating, sedation in some patients
  - Breast cancer risk may vary by type and duration
- **Combined Estrogen–Progestogen Therapy**
  - Breast cancer risk increases with duration of use
  - Thromboembolic risk influenced by formulation and route
  - Ongoing risk–benefit reassessment required

Estrogen

Which one do we choose?

Types

- E1 (Estrone)
  - Weaker
  - More common after menopause
- E2 (**Estradiol**): primary systemic estrogen
  - Strongest
  - Dominant during reproductive years
- E3 (Estriol):
  - Weakest
  - Important in pregnancy
  - Good local effects (minimal systemic absorption)
- E4 (Estetrol)
  - fetal estrogen,
- Synthetic estrogens (mainly estradiol)
  - designed for birth control or hormone therapy
  - have a higher thrombotic risk
- Conjugated equine estrogens
  - Effective, but less physiologic

Estrogen

Risk Depends on Route

Risk Framework

- Oral estrogen = Highest Risk:
  - First-pass hepatic metabolism - > Higher levels due to liver conversion
  - ↑ clotting factors -> higher clot risk: ↑ stroke/VTE risk
  - ↑ triglycerides
- Conjugated equine estrogens
- Transdermal Estradiol
- Vaginal estrogen (E2 or E3) = Lowest Risk
  - minimal systemic absorption
  - Safe with prior VTE
  - Often acceptable in breast cancer survivors

Estrogen

Preferred Systemic Therapy

Estradiol (E2)

- **Gold standard** for menopausal hormone therapy
- Best for hot flashes, bone protection, mood, sleep
- Available as patch, gel, spray, pill, vaginal ring

* preferred delivery: **Transdermal** estradiol (patch, gel, spray) at the **lowest effective dose** for an **individualized duration**

Estrogen

When can you not use it?

Absolute Contraindications

- Active breast cancer
- Prior estrogen-sensitive breast cancer
- Untreated endometrial cancer
- Unprovoked VTE / thrombophilia
- Active clot, stroke, or MI
- Severe liver disease

Progestins

Safety Partner

Some type of progestin is required if the uterus is present:

- Micronized progesterone
- Medroxyprogesterone acetate (MPA)
  - Higher breast and CV risk
- Norethindrone
- Levonorgestrel IUDs
  - Endometrial protection
  - Bleeding control
  - Contraception if needed

Progestins

Preferred Systemic Therapy

Micronized Progesterone

- Improves sleep
- Lower breast/VTE risk vs MPA

Hormonal Management

Additional hormonal medications

FDA Approved

- Prasterone - converts to estrogen and testosterone in the vagina
- Ospemiphine - SERM, agonist in vagina antagonist (blocks) in breast tissue

FDA NOT Approved

Testosterone

- Not FDA approved for women
- Has only been proven to be effective for decreased libido
- Can be beneficial

Case 1
"The Labs Are Normal"

Patient

A 47-year-old woman presents with:

- Night sweats
- New anxiety
- Sleep fragmentation
- Regular menses

Labs: FSH normal, estradiol normal

Question: What is the most appropriate next step?

A. Reassure — labs are normal

B. Start SSRI

C. Transdermal estradiol

D. Repeat labs in 6 month

Case 2
“Clot History”

Patient

A 52-year-old with severe hot flashes

History of provoked DVT after surgery

Uterus intact

Question: Safest treatment option?

A. Oral estradiol

B. Transdermal estradiol + progesterone

C. Ethinyl estradiol

D. No estrogen options

Case 3
“Breast Cancer Fear”

Patient

A 60-year-old breast cancer survivor (ER+)

Severe dyspareunia, recurrent UTIs

No systemic symptoms

Question: Appropriate treatment?

A. No estrogen

B. Systemic estradiol

C. Vaginal estrogen

D. Ospemifene only

Clinical Pearls

Perimenopause

Symptom Driven Prescribing

- Treat symptoms, not lab values
- Match hormone to symptom profile
    - Estrogen is indicated for moderate–severe vasomotor symptoms
- Vaginal estrogen is underused for GU symptoms
- OCPs are OKAY
- Route matters
    - Transdermal estrogen preferred for VTE risk reduction
- Use lowest effective dose & Re-evaluate annually
- Keep in mind contraindications
    - estrogen-dependent cancers, VTE history, active liver disease

Primary care can manage most cases, but refer the following:

- Abnormal uterine bleeding requiring imaging or biopsy
- Severe mood disorders
- Complex medical histories requiring individualized HT
- Persistent or worsening symptoms despite treatment

Clinical Pearls

HRT

What HRT is NOT:

- Not weight-loss therapy – does not replace diet or exercise
- Not primary CV prevention
- Not a fountain of youth
- Not lifelong by default

• Patient Counseling:

- Shared decision-making
- Reassess annually
- Quality-of-life focused

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Questions?