Hormone Therapy's Twin Faces: Sorting Science From Misconception

Kelsey Giara, PharmD, RPh
Freelance Medical Writer
Adjunct Assistant Professor
UConn School of Pharmacy

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Disclosures

Dr. Giara has no financial relationships to disclose related to this content.

Note that this activity will employ the terms "woman/women" to align with the biological expectations of hormone regulation in people assigned female sex at birth.

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Learning Objectives

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

- **Discuss** the clinical evidence on safety, efficacy, and patient outcomes for hormone replacement therapy (HRT), highlighting areas of misconception or confusion
- **Compare** HRT options and bioidenticals, including mechanisms of action, formulations, and regulatory pathways
- **Apply** guidelines and evidence-based recommendations to individualize patient counseling and therapeutic decision-making when managing HRT

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Hormone Physiology

The Roles of Estrogen, Progesterone, and Testosterone

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Estrogen: Mechanisms of Action

- Estrogen acts primarily through nuclear estrogen receptors (ER)
  - **ERα:** uterus, pituitary, liver, bone, mammary
  - **ERβ:** ovary, lung, prostate
- Two major pathways:
  - **Genomic (primary):** estrogen-ER complexes regulate gene transcription through direct DNA binding, tethered interactions, or ligand-independent activation
  - **Rapid, non-genomic:** membrane-associated ERα and GPER1 activate MAPK/ERK and AKT signaling within minutes
- Balance of receptor type, tissue distribution, and signaling pathway determines downstream effects

Hamilton KJ, et al. *Curr Top Dev Biol.* 2017;125:109-146.

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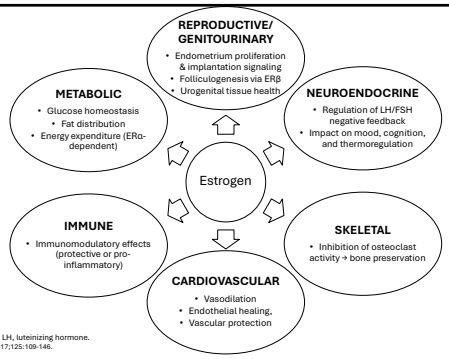
Estrogen: Physiologic Targets



FSH, follicle-stimulating hormone; LH, luteinizing hormone.
Hamilton KJ, et al. *Curr Top Dev Biol.* 2017;125:109-146.

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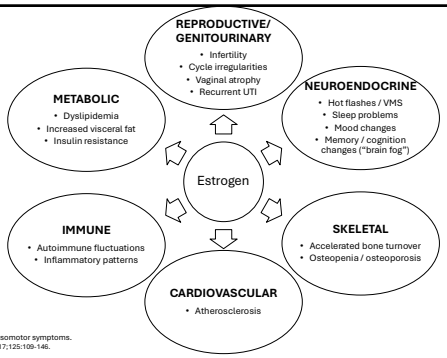
Estrogen: Clinical Symptoms of Deficiency



UTI, urinary tract infection; VMS, vasomotor symptoms.
Hamilton KJ, et al. *Curr Top Dev Biol.* 2017;125:109-146.

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Progesterone: Mechanisms of Action

- Progesterone acts through nuclear and membrane progesterone receptors (PR)
  - **PR-A:** generally, a *repressor* of transcription
  - **PR-B:** stronger *activator* of transcription
  - **PR-C:** truncated form detected in myometrium
- Two major pathways:
  - **Genomic (primary):** progesterone activates nuclear PR, which dimerizes and binds DNA at to control gene transcription; slow onset (hours to days); main regulator of reproductive tissue function
  - **Rapid, non-genomic:** membrane-associated PRs (mPRs) activate fast signaling cascades within seconds to minutes
- Balance of receptor isoforms, tissue distribution, and pathway activation determines physiologic effects

Kolatorova L, et al. *Int J Mol Sci.* 2022;23(14):7989.

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Progesterone: Key Physiologic Roles

Reproductive System (Endometrium & Uterus):
- Stabilizes the endometrium and prevents estrogen-driven overgrowth
- Reduces uterine contractility
- Supports a balanced menstrual cycle

Central Nervous System / Mood / Sleep:
- Metabolites calm the nervous system
- Helps regulate mood, anxiety, and sleep
- Modulates pain sensitivity

Immune Effects:
- Has anti-inflammatory, immune-modulating effects
- Contributes to overall tissue stability in the reproductive tract

Breast Tissue
- Works with estrogen in breast development and cyclic breast changes

Other:
- Can influence fluid balance at high doses
- Affects thermoregulation and sleep quality

Kolatorova L, et al. *Int J Mol Sci.* 2022;23(14):7989.

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Testosterone's Role in Women's Health

Sexual Desire & Arousal
• Primary evidence-based indication for therapy • Strongest associations with low libido
Cognitive Support
• May enhance verbal learning & memory in post-menopause • Neuroprotective actions
Musculoskeletal Health
• Supports lean mass, strength, and bone density • Low levels linked to accelerated bone loss
Cardiovascular Physiology
• Favorable effects on vascular tone & endothelial function
Vulvovaginal Tissue Effects
• Androgen receptors present in vaginal epithelium • May improve atrophy and sexual comfort

Davis SR, Wahlin-Jacobsen S. *Lancet Diabetes Endocrinol.* 2015;3(12):980-992.

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What is Menopause?

Perimenopause
- Occurs 3-5 years before menopause
- Typically begins in mid-to-late forties
- Estrogen and progesterone levels begin to fluctuate
- Initial symptoms begin (mood changes, irregular menstrual cycles, etc.)

Menopausal transition usually lasts about 7 years but can be as long as 14 years.

Menopause
- Average age is 51, but varies greatly
- Absence of menses for 12 months straight without other causes
- No longer able to become pregnant

Postmenopause
- Signals end of reproductive years
- Ovaries continue to produce low levels of estrogen/progesterone, but ovulation and menstruation cease

Ferris E. Preparing for Menopause: Understanding the Signs and Symptoms in all Three Stages. Accessed Nov. 18, 2025. https://www.summahealth.org/flourish/entries/2023/04/preparing-for-menopause-understanding-the-signs-and-symptoms-in-all-three-stages; NIH. What is menopause? Accessed Nov. 18, 2025. https://www.nia.nih.gov/health/menopause/what-menopause

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Vasomotor Symptoms (VMS)

- Hot flushes (or flashes) and night sweats
  - Sudden sensation of extreme heat in the upper body, particularly the face, chest, and neck
  - Perspiration, flushing, chills, clamminess, anxiety, and possible heart palpitations
  - Last about 1 to 5 minutes
- Symptoms are debilitating and interfere with quality of life and sleep
  - 87% of women who have hot flushes have them daily
  - One-third experience more than 10 episodes daily
- Associated with increased blood pressure and clinical hypertension
- Up to 82% of women during and/or after the menopause transition
  - For about half of women, persists for 4 years after menopause
  - For 10% of women, lasts 12 years following menopause

Lee E, et al. *Am J Physiol Heart Circ Physiol.* 2022;323(6):H1270-H1280.; ACOG. *Obstet Gynecol.* 2014;123(1):202-216.

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Genitourinary Syndrome of Menopause (GSM)

- Genitourinary syndrome of menopause (GSM) is a chronic, progressive, vulvovaginal, sexual, and lower urinary tract condition
- Affects up to 70% of postmenopausal and 15% of premenopausal women
  - Often undiagnosed, as symptoms are mild and nonspecific in about half of postmenopausal women
- Decreased estrogen results in hormonal and anatomical changes in the genitourinary tract
- Greatly impacts quality of life, especially for sexually-active women

Angelous K, et al. *Cureus*. 2020;12(4):e7586.

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GSM Pathophysiology

Decreased estrogen results in hormonal and anatomical changes in the genitourinary tract

Changes in External Genitalia:	Changes in Vaginal Health:	Pelvic Floor and Vaginal Issues:
• Loss of labial and vulval thickness • Reduced pubic hair and subcutaneous fat of labia majora • Reduced labia minora and hymenal remnants	• Decreased collagen, elasticity, and blood flow • Reduced vaginal discharge • Dry and thin epithelium • Change in vaginal microbiome and ↑ pH	• Decreased pelvic floor strength and control • Short and narrow vagina • Prolapse

Angelous K, et al. Cureus. 2020;12(4):e7586.

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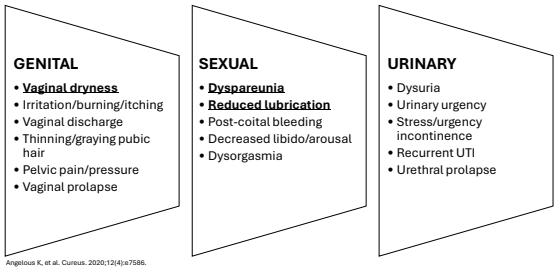
Symptoms of GSM



Angelous K, et al. Cureus. 2020;12(4):e7586.

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Early or Non-Natural Menopause

- **Premature Ovarian Insufficiency (POI)**
  - Loss of ovarian function before age 40
  - Leads to estrogen deficiency with increased risks for osteoporosis, CVD, and mood/cognitive symptoms
- **Early Menopause**
  - Natural cessation of menses before age 45
  - Similar symptoms to typical menopause but with greater long-term health risks
- **Surgical Menopause**
  - Bilateral oophorectomy (BO; ovary removal) ± hysterectomy (uterus removal)
  - Immediate, abrupt estrogen loss , leading to more intense VMS and GSM
- **Iatrogenic or Treatment-Induced Menopause**
  - Chemotherapy, pelvic radiation, or GnRH agonists/antagonists
  - Can cause temporary or permanent ovarian suppression

CVD, cardiovascular disease; GnRH, gonadotropin releasing hormone.

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Understanding Hormone Replacement Therapy

Guidelines, Formulations, and Safety Considerations

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What is Hormone Replacement Therapy (HRT)?

- Estrogen alone or in combination with progesterone to replenish ovarian hormones diminished during the menopausal transition
- Alleviates associated symptoms, most commonly VMS, sleep, mood, GSM, and bone health
- Considered when symptoms impair quality of life and benefits outweigh risks
  - Therapy should be individualized based on symptoms and risk-benefit profile
- **When and why are progestins added?**
  - When systemic estrogen is given to a woman with a uterus, a progestin is required
  - Prevents estrogen-induced endometrial hyperplasia and cancer
  - May also modestly improve VMS, but not used as monotherapy

ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.

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Bioidentical vs. Synthetic Hormones

- **Bioidentical hormones** are chemically identical to human hormones
  - Approved through the standardized NDA pathway
  - Predictable pharmacokinetics and receptor activity identical to natural hormones
- **Synthetic hormones** are structurally modified versions of human hormones
  - Used in many FDA-approved estrogen-progestin regimens
  - Altered molecular structure may change receptor binding, metabolic effects, and AE profiles
  - May offer longer half-life, stronger potency, or specific therapeutic advantages

AE, adverse effect.
ACOG. *Obstet Gynecol*. 2023;142(5):1266-1273.

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Guidelines and Recommendations

- **FDA-approved indications:**
  - Moderate-to-severe VMS
  - Osteoporosis prevention in postmenopausal women
  - Treatment of hypoestrogenism caused by hypogonadism, BO, or POI
  - Moderate-to-severe vulvovaginal symptoms
- **ACOG/NAMS Guidance:**
  - Use lowest effective dose for the shortest duration to balance symptom control with risks
  - About half of women experience recurrent hot flashes upon discontinuation
  - Reassess at least annually and continue only if benefits outweigh risks

Women's Health Initiative (WHI) is a massive NIH-funded set of trials that profoundly shaped modern understanding of HRT risks.

ACOG, American College of Obstetricians and Gynecologists; NAMS, North American Menopause Society.
ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.

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Fact OR Fiction?

Women who enter menopause early (before age 50) should avoid HRT due to increased risks.

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"Window of Opportunity" for HRT

Best benefit-risk when started before 60 years old or within 10 years of menopause

- Reanalysis of WHI data suggests possible cardioprotection in this younger, early-start group
- Early post-menopause, estrogen is cardioprotective
  - Estrogen upregulates ERα in blood vessels, improving vascular health and slowing atherosclerosis progression
- Late post-menopause, estrogen loses benefit due to iron accumulation
  - ~ Age 65, iron accumulates in vascular tissues, increasing ferritin and downregulating ERα
  - Estrogen + high iron → further ERα degradation, shifting estrogen's role from protective to pro-atherosclerotic
- Starting later leads to higher absolute risks
  - CHD, stroke, VTE, dementia

CHD, coronary heart disease; VTE, venous thromboembolism.
ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.; Xu T, et al. *Elife*. 2023;12:e80494.

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Fact OR Fiction?

There is no mandatory age at which women must stop HRT.

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Other Indications for HRT

- To prevent osteoporosis
- To initiate puberty in adolescents with primary amenorrhea
- As part of a gender transition
- To treat some types of cancer or to relieve some cancer symptoms
- To treat infertility in certain situations

ACOG. Hormone Therapy for Menopause. Accessed Nov. 18, 2025. https://www.acog.org/womens-health/faqs/hormone-therapy-for-menopause

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Fact OR Fiction?

Women with a uterus always require a progestin when using any form of estrogen.

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Who Gets What, and Why?

- **Systemic HRT:**
  - **Who?** Women with VMS (hot flashes, night sweats), with or without vaginal symptoms
  - **Why?** Systemic estrogen is required to treat VMS; local estrogen is ineffective for this purpose
- **Local HRT:**
  - **Who?** Women with isolated GSM (vaginal dryness, dyspareunia, atrophy)
  - **Why?** Local therapy effectively treats vaginal symptoms with minimal systemic absorption and does not require progestin
- **NO HRT:**
  - History of breast or endometrial cancer, stroke, heart attack, blood clots, or liver disease

ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.

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Estrogen HRT Formulations

Estrogen	Route	Typical Dosing	Notes
Conjugated equine estrogens (CEE)	Oral	0.625 mg/day	Standard systemic option
Estradiol-17β *(bioidentical)*	Oral	1 mg/day	Widely used; effective for VMS
	Topical (gel, cream spray)	Low dose (varies)	Systemic absorption; treats VMS and requires progestin in patients with a uterus
	Transdermal (patch)	0.0375–0.05 mg/day	Lower VTE risk vs oral
	Vaginal (tablet, ring, cream)	Local doses (product-specific)	For GSM only, *not* VMS; no progestin needed
Ethinyl estradiol	Oral	5 mcg/day	Low-dose systemic formulation; rarely used in HRT

VTE, venous thromboembolism.
ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.

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Progestins in HRT

- **Bioidentical: micronized progesterone (MP)**
  - May be less thrombogenic than synthetic progestins
  - Often preferred for endometrial protection due to better tolerability and metabolic profile
- **Synthetic:**
  - Medroxyprogesterone acetate (MPA)
  - Norethindrone acetate (NETA)
  - Levonorgestrel (LNG); IUD used off-label for endometrial protection
- Can be used daily or cyclically
  - 12 to 14 days per month needed to ensure endometrial protection
- May improve VMS symptoms but not recommended as monotherapy

IUD, intrauterine device.
ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.

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Fact OR Fiction?

Women using a selective estrogen receptor modulator do not require progestin therapy.

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SERMs and TSECs: No Progestin Necessary

SELECTIVE ESTROGEN RECEPTOR MODULATOR (SERM)

- **Ospemifene 60 mg once daily**
  - FDA approved for symptoms of vulvar and vaginal atrophy (severe dyspareunia or vaginal dryness)
- Provide estrogen benefits to vaginal tissue while blocking estrogen effects elsewhere
- Oral option for dyspareunia/GSM in women not using systemic estrogen

TISSUE-SELECTIVE ESTROGEN COMPLEX (TSEC)

- **CEE/bazedoxifene 0.45 mg/20 mg daily**
  - FDA approved for VMS treatment and postmenopausal osteoporosis prevention
- Provides estrogenic benefits plus SERM-mediated tissue protection
- Useful in women who cannot tolerate or prefer to avoid progestins

ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.; Osphena (prescribing information). Duchesnay Inc.;2025.; Duavee (prescribing information). Pfizer, Inc.;2024.

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HRT Risks: Venous Thromboembolism (VTE)

1. **Estrogen first pass through the liver**
   - Absorbed through GI tract and enters the liver via the portal circulation
   - High, concentrated exposure stimulates hepatic protein synthesis
2. **Upregulation of procoagulant factors**
   - Fibrinogen
   - Prothrombin (Factor II)
   - Factors VII, VIII, IX, and X
   - von Willebrand factor
3. **Suppression of natural anticoagulants**
   - Protein S
   - Antithrombin (mildly)
   - Activated protein C (functional resistance increases)

Prothrombotic state and increased VTE risk

GI, gastrointestinal.
ACOG. *Obstet Gynecol*. 2013;121(4):887-890.

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HRT Risks: Cancer

Endometrial cancer:
- Systemic estrogen stimulates endometrial proliferation
- Unopposed estrogen in women with a uterus *increases* risk of endometrial hyperplasia and cancer
- Adding a progestin (or an estrogen/SERM combination) provides endometrial protection

Breast cancer:
- Combined estrogen-progestin therapy is associated with a small *increase* in breast cancer risk
- Driven by the progestin component; estrogen-only does not increase breast cancer risk
- Risk increases with longer duration of combined therapy

Colon cancer:
- Combined estrogen-progestin therapy is associated with a *reduced* colorectal cancer risk
- Protective effect is specific to the combination regimen, not estrogen monotherapy

ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.

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Other Risks of HRT

- **Stroke:** Slight increase with oral estrogen; estrogen alone has neutral/low effect in younger women
- **Coronary heart disease (CHD):** Small increase with CEE+MPA; neutral/decreased risk with estrogen alone initiated in early menopause
- **Gallbladder disease:** Oral estrogen increases risk of gallstones and cholecystitis
- **Urinary incontinence:** Oral estrogen may worsen stress and mixed incontinence
- **Dementia (≥ 65 yrs):** WHI Memory Study showed increased risk with CEE+MPA started after age 65
- **Ovarian cancer:** Slight increase with long-term estrogen-only therapy (> 5-10 years), but data is inconsistent

ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.

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How HRT Regimen Impacts Safety

Route & VTE Risk	Oral estrogen → highest VTE risk Transdermal estrogen → lower VTE risk Vaginal estrogen → no association with VTE
Regimen & Breast Cancer Risk	Estrogen + progestin → increased breast cancer risk Estrogen alone → no increased breast cancer risk
Dose and Duration	Higher systemic doses → more symptom relief but potentially greater VTE and breast cancer risks ACOG/NAMS recommendation: Use the lowest effective dose for the shortest duration to balance symptom control with risks

ACOG. *Obstet Gynecol*. 2014;123(1):202-216.

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Testosterone's Role

- Directly binds androgen receptors
- Responsible for libido, sexual responsiveness, energy, and musculoskeletal effects
- Only evidence-based indication is hypoactive sexual desire disorder (HSDD) in postmenopausal women
- No FDA-approved testosterone product in the U.S. for women
  - Strongest evidence for off-label, low-dose transdermal testosterone adapted from male products *with careful monitoring*
  - Oral testosterone, pellets, injections, and compounded products NOT recommended due to safety concerns and lack of FDA approval
- Goal is to keep testosterone in the physiologic premenopausal female range
- Potential AEs (dose-related): acne, hirsutism, voice changes (rare, may be irreversible), lipid changes
  - Long-term safety data remain limited

ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.

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Fact OR Fiction?

Custom-compounded bioidentical hormones are the safest option for HRT.

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Compounded Bioidenticals

- Custom-mixed products prepared by compounding pharmacies
  - Estradiol, progesterone, testosterone, DHEA, combinations
  - Not FDA approved; no required proof of safety, efficacy, bioavailability, potency, or consistency
- Not preferred from a regulatory or safety standpoint
  - Should not replace FDA-approved products
- A pharmacist or prescriber may choose them for various reasons:
  - Custom strengths or hormone ratios unavailable commercially
  - Alternative dosage forms (troches, sublingual, vaginal combos)
  - Avoid dyes/excipients causing intolerance or allergy
  - Cost or insurance access issues
  - Patient preference for customizable formulations

Use ONLY when:
- Needed dose, formulation, or combination is not commercially available
- Patient has documented excipient allergy or intolerance
- Special clinical titration is required
- Decision is made with informed consent and safety monitoring

DHEA, dehydroepiandrosterone.
ACOG. *Obstet Gynecol*. 2014;123(1):202-216.; NAMS. *Menopause*. 2022;29(7):767-794.

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Real-World Applications

Shared Decision-Making, Misconceptions, and Applying the Evidence

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Why is HRT So Controversial?

- In 2002, WHI data reported an increased risk of CVD, stroke, and breast cancer in women who took estrogen and a synthetic progestin for > 5 years
  - 70% of participants were > 60 years old, not newly menopausal women
  - All took only one type of HRT (CEE + MPA)
  - Designed as a chronic disease prevention study, rather than symptom relief
- Media misrepresented the data, causing many women to suffer unnecessarily
- Since 2003, systemic estrogen ± progestin products for menopause carried a Boxed Warning highlighting increased risks of:
  - CVD and stroke
  - VTE
  - Invasive breast cancer
  - Probable dementia in women ≥ 65 years old

Rossouw JE, et al. *JAMA*. 2002;288(3):321-333.; FDA. FDA Requests Labeling Changes Related to Safety Information to Clarify the Benefit/Risk Considerations for Menopausal Hormone Therapies. Nov. 19, 2025. https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-labeling-changes-related-safety-information-clarify-benefitrisk-considerations

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FDA Reconsidered These Warnings

- FDA announced it will remove WHI-era warning language
- Based on a comprehensive review of newer data:
  - Reanalysis of WHI stratified by age and time since menopause
  - Observational and trial data showing favorable benefit-risk for healthy women < 60 years old or < 10 years since menopause
  - Data showing very low systemic risk with low-dose vaginal estrogen
- Also recognized that the old Boxed Warning
  - Was based on older women starting HRT late
  - Overstated risk for typical candidates (symptomatic women in their 50s)
  - Deterred appropriate treatment, especially low-dose vaginal estrogen
- Ultimately contributing to underutilization
  - About one-third of women aged 45 to 65 years experiences moderate to severe VMS
  - Less than 5% of women in this age range were prescribed HRT in 2020

FDA. FDA Requests Labeling Changes Related to Safety Information to Clarify the Benefit/Risk Considerations for Menopausal Hormone Therapies. Nov. 19, 2025. https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-labeling-changes-related-safety-information-clarify-benefitrisk-considerations

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Fact OR Fiction?

FDA removed all Boxed Warnings from HRT products, as new evidence shows it no longer carries significant risks.

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Updated Safety Labeling: November 2025 (cont.)

Boxed Warning changes:

- **Remove:**
  - Language related to CVD, breast cancer, and probable dementia
  - Language related to endometrial cancer except in the systemic estrogen-alone drugs
  - Recommendation to use the lowest effective dose for the shortest amount of time
- **Retain:**
  - Endometrial cancer warning for systemic estrogen-alone products

Overall labeling changes:

- **Remove:**
  - Probable dementia warning
- **Add:**
  - Consideration of starting HRT for VMS in women < 60 years old or < 10 years since menopause
  - WHI data in women 50-59 years old
- **Retain:**
  - Information about CVD and breast cancer warnings

FDA. FDA Requests Labeling Changes Related to Safety Information to Clarify the Benefit/Risk Considerations for Menopausal Hormone Therapies. Nov. 19, 2025. https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-labeling-changes-related-safety-information-clarify-benefitrisk-considerations

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Fact OR Fiction?

Nonhormonal alternatives are available and equally as effective as HRT.

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Non-Hormonal Alternatives

VMS	GSM

• Elinzanetant (NK1/NK3 receptor antagonist; FDA approved)
• Fezolinetant (NK3 receptor antagonist; FDA approved)
• SSRIs/SNRIs
  • Paroxetine 7.5 mg (FDA approved)
  • Others off-label
• Gabapentin (off-label)
• Clonidine (off-label)
	• Vaginal moisturizers (regular use)
	• Vaginal lubricants (before intercourse)
	• Ospemifene (SERM; FDA approved for dyspareunia)
	• Prasterone (vaginal DHEA; FDA approved for dyspareunia)

NK, neurokinin; SNRI, serotonin-norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors.
ACOG. *Obstet Gynecol.* 2014;123(1):202-216.; NAMS. *Menopause.* 2022;29(7):767-794.; Lynkuet (prescribing information). Bayer HealthCare Pharmaceuticals Inc.;2025.; Veozah (prescribing information). Astellas Pharma US, Inc.;2024.

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Dehydroepiandrosterone (DHEA) in Menopause

- A precursor hormone (prohormone) converted in peripheral tissues into testosterone and estradiol
- **Prasterone 6.5 mg**
  - Vaginal DHEA inserts
  - FDA approved for moderate to severe dyspareunia due to GSM
  - Acts locally in vaginal tissues (DHEA → androgens → estrogens) to improve lubrication and tissue health
- Oral DHEA supplements are not FDA-approved or recommended by NAMS or ACOG
  - Inconsistent evidence, variable purity (supplement, not regulated as a drug), unpredictable conversion to sex hormones
  - Acne, hirsutism, mood changes at higher doses

ACOG. *Obstet Gynecol.* 2014;123(1):202-216.; NAMS. *Menopause.* 2022;29(7):767-794.; Intrarosa (prescribing information). AMAG Pharmaceuticals;2018.

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Shared Decision-Making

Integrates clinical evidence with patient preferences, ensuring HRT is personalized, safe, and aligned with each patient's goals.

1. **Clarify Patient Goals:** VMS relief, GSM symptom management, mood/sleep improvement, bone health, minimizing medication burden or risks
2. **Review Individual Risk Profile:** Age & time since menopause; VTE, stroke, breast cancer, CVD risks; contraindications; personal/family history
3. **Present Evidence-Based Options:** Systemic vs local estrogen, FDA-approved bioidentical hormones, TSEC if avoiding progestins, progestin choices, nonhormonal alternatives
4. **Discuss Benefits vs Risks Transparently:** VTE & cancer risks differ by route, timing, formulation; lowest effective dose and shortest needed duration; annual reevaluation
5. **Incorporate Patient Preferences:** Formulation (patch, pill, gel, ring); counsel on FDA-approved vs compounded bioidenticals; cost, insurance, convenience, lifestyle

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Broaching A Sensitive Subject

- **Acknowledge the Sensitivity and Validate Experiences**
  - Menopause, aging, sexuality, and hormones can feel personal, stigmatized, or emotionally charged for many women
  - "Your symptoms are real and deserve treatment."
  - "There's no 'right age' or 'right way' to manage menopause—we'll tailor this to you."
- **Reduce Stigma**
  - Emphasize menopause as a normal physiologic transition, not a failure or loss.
  - Frame HRT as "symptom relief" or "hormone replacement" rather than "fixing" aging.
- **Use Open, Nonjudgmental Questions**
  - "How are your symptoms affecting your day-to-day life?"
  - "What concerns do you have about hormone therapy or treatments?"
  - "Have you heard anything about HRT from friends or social media that you'd like to clarify?"
- **Emphasize Shared Decision-Making**
  - Present HRT as one of several evidence-based options, not a mandate.
  - Focus on goals: symptom relief, quality of life, sexual health, sleep, long-term health.

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Responding to Common Concerns

Patient Concern	Clarify
"I heard HRT causes breast cancer."	"Risk depends on the type of hormone, timing, and individual factors. We'll choose the safest option for your situation, and many women are good candidates."
"I don't want to gain weight."	"Midlife weight changes are age-related, not caused by hormone therapy. HRT may actually improve sleep and energy, which supports weight stability."
"I'm afraid of taking hormones."	"These are physiologic doses of the same hormones your body used to make. We can use the lowest effective dose and revisit how you feel regularly."
"Isn't it safer to use bioidentical hormones?"	"FDA-approved estradiol and micronized progesterone are already bioidentical, meaning they are chemically identical to the hormones your body naturally makes. These products have consistent dosing and have been thoroughly tested for safety."
"I'm worried my symptoms will come back if I stop."	"About half of women have symptoms return, whether they stop gradually or suddenly. If that happens, we can adjust the plan—you're not stuck with one option."

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Key Takeaways

- Hormone therapy is the most effective treatment for VMS, with safety shaped by timing, dose, type, and route
- FDA-approved estradiol and micronized progesterone are bioidentical; compounded products lack FDA oversight and should be used only when necessary.
- Progestin is needed only with systemic estrogen in women with a uterus, not with low-dose vaginal estrogen.
- Route matters: transdermal estrogen carries lower VTE risk and may be safer for many women.
- Shared decision-making—validating concerns, correcting misinformation, and aligning therapy with goals—is central to patient-centered menopause care.

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THANK YOU!

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