# What's New in Menopause Management: Innovations and Evolving Practices

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# Objectives

- Review recent advancements in menopause management
- Explore innovative therapies and non-hormonal options
- Understand updated clinical guidelines
- Apply individualized, evidence-based strategies for symptom management

# Menopause by the Numbers in US

- 6,000 women reach menopause every day
- 1.3 million women enter menopause each year
- Average age of menopause: 51 years (range: 45–56)
- Symptom prevalence:
  - 80–90% experience at least one bothersome symptom
  - 81% report hot flashes
  - 80% report night sweats
- Duration of symptoms: Average 7.4 years, can last up to 14 years
- Workforce impact:
  - Women aged 45–60 make up 20% of the U.S. female workforce
  - 10.8% miss work due to symptoms
- Economic burden:
  - U.S. annual productivity loss: $1.8 billion
  - Healthcare costs: $24.8 billion
  - Total annual economic impact: $26.6 billion

# Global Numbers

- 1.2 billion women worldwide will be menopausal or postmenopausal by 2030
- By 2030, 47 million women will enter menopause each year globally
- Premature menopause (<40 years) affects 1% of women
- Early menopause (40–45 years) affects 5% of women

# Overview of Menopause

- Permanent cessation of menstruation for 12 months due to ovarian follicle depletion
- Average age: 51 years (range 45–55)
- Most common symptoms: Vasomotor (hot flashes, night sweats), genitourinary (vaginal dryness, urinary symptoms), mood changes, sleep disturbances

# Menopausal Health Implications

- Bone health
  - Increased risk of osteoporosis and fractures
- Cardiovascular health
  - Risk rises after menopause due to estrogen decline
- Metabolic changes
  - Weight gain, insulin resistance
- Cognitive and mood
  - Possible memory changes, depression, anxiety

# Genitourinary Syndrome of Menopause (GSM)

- Collection of symptoms and signs associated with decreased estrogen and other sex steroids
- Affecting the genital, urinary, and sexual health of menopausal women.
- Common GSM Symptoms
  - Vaginal dryness
  - Burning
  - Irritation
  - Painful intercourse (dyspareunia)
  - Urinary issues (urgency, frequency, recurrent UTIs)

# HRT vs MRT

## Hormone Replacement Therapy

- Use of estrogen (with or without progestogen) to relieve menopausal symptoms.
- Indications
  - Moderate to severe vasomotor symptoms
  - Genitourinary Syndrome of Menopause (GSM)
  - Prevention of osteoporosis in high-risk women
- Forms: Oral, transdermal, vaginal
- Benefits
  - Most effective for hot flashes and night sweats
  - Improves GSM symptoms
- Risks
  - VTE
  - Stroke (higher with oral estrogen)
  - Breast cancer risk with combined therapy (long-term use)

## Menopausal Replacement Therapy

- Often used interchangeably with HRT, but sometimes refers to more holistic, broader, individualized therapy, including:
  - Hormonal treatments
  - Non-hormonal medications
  - Lifestyle interventions
- Goal: Comprehensive symptom management and long-term health optimization.
- Includes:
  - HRT
  - Non-hormonal drugs (SSRIs, gabapentin, NK3 antagonists)
  - Lifestyle medicine (nutrition, exercise, stress reduction)

# Women's Health Initiative (WHI) Timeline

- 1991-1993: WHI launched by NIH to study disease prevention in postmenopausal women
  - Included hormone therapy trials (estrogen alone and estrogen  AND progestin).
- July 2002: WHI combined estrogen  AND progestin trial halted early
  - Stopped due to increased risks of breast cancer, coronary heart disease, stroke, and venous thromboembolism.
- 2004: Estrogen-alone arm stopped after findings of increased stroke risk and no cardiovascular benefit.
- 2002-2003: WHI results widely publicized; HRT prescribing plummeted.
  - FDA mandated boxed warnings on estrogen and progestogen products citing risks of cardiovascular disease, breast cancer, thromboembolism, and probable dementia.
- 2010s: Re-analysis introduced the "timing hypothesis"
  - Benefit-risk profile differs if HRT is started within 10 years of menopause onset.
- 2017-2020: Long-term WHI follow-up confirmed nuanced risks
  - Combined therapy increases breast cancer incidence and mortality
  - Estrogen-alone lowers breast cancer risk but raises stroke risk

# What did Black Box Warning say?

- 2003: FDA applied class-wide boxed warnings for systemic estrogen and estrogen-progestin products based on WHI findings
- Warnings included:
  - Breast cancer (especially with combined therapy)
  - Cardiovascular disease (heart attack, stroke, blood clots)
  - Probable dementia in older women
- These warnings persisted for over 20 years, despite evolving evidence showing risks were overstated for younger women and modern formulations

# 2025 ACTION on Black Box Warning for HRT!

- Nov 10, 2025---FDA announced removal of most black box warnings from menopausal HRT products after comprehensive review and expert panel input
- Risks for cardiovascular disease, breast cancer, and dementia will be removed from boxed warnings and moved to standard labeling
- Endometrial cancer warning remains for estrogen-only systemic therapy.
- Rationale---WHI participants were older (average age 63) and used formulations no longer common
- Newer studies show HRT started within 10 years of menopause or before age 60 has favorable benefit-risk profile
  - Symptom relief, bone health, and possible cognitive benefits
- FDA now recommends individualized decision-making and updated labeling to reflect current science

# Advances in HRT

- Individualized therapy based on age, risk profile
- Transdermal estrogen reduces clot risk compared to oral
- Low-dose regimens for symptom control
- Bioidentical hormones gaining popularity

# Individualized therapy

- Current guidelines (NAMS, ACOG, NICE) emphasize personalized treatment
- Best benefit-risk profile occurs when HRT is started within 10 years of menopause onset or before age 60
- Consider cardiovascular risk, breast cancer history, thromboembolism risk, and patient preferences before initiating therapy

# Transdermal estrogen

- Multiple formulations: patch, gel, or spray
- First-pass liver metabolism which lowers impact on clotting factors
- Reduced risk of venous thromboembolism (VTE) compared to oral estrogen
- Preferred for women with higher VTE risk, obesity, or metabolic syndrome

# Prescribing Transdermal Best Practices

- Patient Selection
  - Higher VTE risk (personal or family history of clotting, obesity, metabolic syndrome)
  - Migraine with aura or elevated triglycerides (oral estrogen can worsen these)
  - Liver concerns (transdermal avoids first-pass metabolism).
- Formulation and Dosing
  - Available as patches, gels, sprays
  - Start with lowest effective dose to control symptoms
  - Common starting dose: estradiol patch 0.025–0.05 mg/day
  - Adjust based on symptom relief and side effects.
- Safety Advantages
  - Bypasses liver metabolism which reduces impact on clotting factors
  - Risk of venous thromboembolism (VTE) compared to oral estrogen
  - Less effect on triglycerides and C-reactive protein.
- Monitoring and Counseling
  - Review symptom control, side effects, and adherence at 3 months, then annually
  - Discuss skin reactions (patch site irritation) and proper application
  - If uterus is present, add progestogen (oral micronized progesterone or LNG-IUS) to prevent endometrial hyperplasia.

# Examples of Transdermal Estrogen Preparations

| Formulation | Examples | Typical Starting Dose | Frequency | Notes |
|---|---|---|---|---|
| **Patch** | Estradiol (Climara, Vivelle-Dot, Minivelle) | 0.025–0.05 mg/day | Once or twice weekly | Most widely used; rotate sites to avoid irritation |
| **Gel** | EstroGel, Divigel | 0.75–1.25 mg/day | Daily | Apply to clean, dry skin; avoid washing area for several hours |
| **Spray** | Evamist | 1 spray (1.53 mg estradiol) | Daily | Apply to inner forearm; allow to dry completely |
| **Combination Patch** | Estradiol + Progestin (CombiPatch) | 0.05 mg estradiol + 0.14 mg norethindrone | Twice weekly | For women with intact uterus |

# Low-dose regimens

- Modern practice favors lowest effective dose for shortest duration to manage vasomotor symptoms
- Low-dose systemic estrogen combined with progestogen (if uterus present) can relieve symptoms while minimizing risks
- Ultra-low-dose options are available for women with mild symptoms or those transitioning off therapy

# Bioidentical hormones

- FDA-approved bioidentical hormones (e.g., micronized progesterone, estradiol) are widely used and considered safe when prescribed in regulated doses.
- Compounded bioidentical hormones are not recommended by major societies (NAMS, ACOG)
  - Lack of FDA oversight
  - Variability in dosing and purity.
- Educate patients on the difference between FDA-approved vs compounded products.

# What to know about Compounding Hormones?

- Custom-mixed by pharmacies
- Not FDA-regulated causes variability in dose and quality
- Major societies (NAMS, ACOG) do NOT recommend compounded products unless no commercial alternative exists
- Avoid saliva or blood hormone testing for dose adjustment as not evidence-based
- Educate patients that “Bioidentical” does not mean safer
- Risks (breast cancer, VTE) are similar to other hormone therapies.

# Non-Hormonal Treatment Options for Menopause

| Category | Examples | Primary Indication | Key Notes |
|---|---|---|---|
| **SSRIs/SNRIs** | Paroxetine, Venlafaxine, Escitalopram | Vasomotor symptoms (hot flashes) | FDA-approved low-dose paroxetine for hot flashes; monitor for mood effects. |
| **Anticonvulsant** | Gabapentin | Vasomotor symptoms, sleep disturbance | Useful for night sweats; often taken at bedtime due to sedative effect. |
| **Alpha-agonist** | Clonidine | Vasomotor symptoms | Less effective than SSRIs/SNRIs; monitor for hypotension and dry mouth. |
| **Neurokinin-3 Receptor Antagonists** | Fezolinetant (Veozah), Elinzanetant | Vasomotor symptoms | New FDA-approved class; non-hormonal, targets hypothalamic thermoregulation. |
| **Local Non-Hormonal GSM Treatments** | Vaginal moisturizers, lubricants | Genitourinary Syndrome of Menopause | First-line for GSM; safe for patients with hormone-sensitive cancers. |

# Lifestyle Modifications---Diet and Exercise

- Regular Physical Activity
  - Aerobic exercise (walking, cycling, swimming)
  - Resistance training (weights, bands)
  - Mind-body practices (yoga, tai chi)
  - Benefits: Reduces frequency and severity of hot flashes (moderate evidence)
    - Improves mood, sleep, and quality of life
    - Maintains bone density and muscle mass
    - Supports weight management
- Healthy Diet
  - Mediterranean-style diet
    - Rich in vegetables, fruits, whole grains, legumes, healthy fats
  - Protein intake
    - 1.0–1.2 g/kg/day to prevent sarcopenia
  - Calcium & Vitamin D
    - For bone health
  - Limit triggers:
    - Alcohol, caffeine, spicy foods (may worsen hot flashes)

# Lifestyle Modifications---Others

- Weight Management
  - Weight loss can reduce vasomotor symptoms
- Stress Reduction
  - Cognitive Behavioral Therapy (CBT)
  - Mindfulness meditation, yoga and relaxation techniques
  - Reduces bother and interference of vasomotor symptomsl
  - Improves sleep and mood
- Avoid Triggers
  - Quit smoking (linked to earlier menopause and worse symptoms)
  - Limit alcohol (hot flash trigger, bone health risk)
- Sleep Hygiene
  - Maintain consistent schedule
  - Cool, dark bedroom
  - Limit caffeine and alcohol (increases insomnia and night sweats)

# Innovations and Emerging Therapies

- Tissue-selective estrogen complexes (TSECs)
  - SERMs combined with estrogen for tailored therapy
- Local Preparations
  - Vaginal DHEA
  - Testosterone
- Digital health tools for symptom tracking and telehealth

# Tissue-Selective Estrogen Complexes (TSECs)

- TSECs combine conjugated estrogens with a Selective Estrogen Receptor Modulator (SERM) (e.g., bazedoxifene)
- Purpose
  - Provide estrogen's benefits (relief of vasomotor symptoms, bone protection)
  - Avoid need for progestin in women with a uterus
  - Reduce risk of endometrial hyperplasia and breast stimulation
- Benefits
  - Improves hot flashes and GSM
  - Maintains bone density
  - Lower risk of abnormal uterine bleeding compared to traditional estrogen-progestin therapy

# Local Preparations

- Local Testosterone
  - Enhances libido and sexual function
  - Often used in compounded creams for clitoral/vulvar application
  - Improves arousal, orgasm, and urinary health
- Vaginal DHEA
  - Restores vaginal elasticity and lubrication
  - Improves GSM symptoms (dryness, dyspareunia)
  - Minimal systemic absorption → safe for women who cannot use systemic estrogen

# Digital Health Tools

- Apps for symptom tracking and education (Elektra, Olivia, Vitelle)
- Telemedicine platforms offering personalized HRT and non-hormonal care
- Virtual CBT programs for mood and sleep
- Benefits:
  - Improves access to menopause specialists
  - Enables personalized care plans
  - Empowers patients through data-driven insights

# Evolving Clinical Guidelines

- NAMS 2023 Position Statements
  - North American Menopause Society
  - Now called “The Menopause Society”
  - Non hormonal options for symptoms management
- ACOG 2024 Guidelines
  - American College of Obstetricians and Gynecologists
  - Emphasis on personalized care
- NICE 2024 Updates
  - National Institute for Health and Care Excellence
  - UK-based organization that develops evidence-based guidelines and recommendations for health, public health, and social care to improve outcomes and ensure best practices
  - Holistic approach

# NAMS 2023---Top 3 Takeaways

- Hormone Therapy Remains the Gold Standard
  - Still the most effective treatment for vasomotor symptoms (VMS) such as hot flashes and night sweats..
  - Recommended for women within 10 years of menopause onset or under age 60, provided there are no contraindications (e.g., estrogen-sensitive cancers, cardiovascular disease)
- Evidence-Based Nonhormone Therapies
  - Recommended for women who cannot or choose not to use HT
    - Cognitive-behavioral therapy (CBT) and clinical hypnosis (mind-body techniques)
    - Prescription medications
      - SSRIs/SNRIs (e.g., paroxetine, venlafaxine)
      - Gabapentin
      - Oxybutynin
      - Fezolinetant (a newly FDA-approved neurokinin-3 receptor antagonist)
- Therapies Not Recommended
  - The statement explicitly advises against certain interventions due to insufficient or poor evidence
    - Lifestyle approaches: cooling techniques, avoiding triggers, exercise, yoga.
    - Dietary supplements and herbal remedies: soy products, cannabinoids.
    - Other interventions: acupuncture, chiropractic, clonidine, pregabalin

# ACOG 2024 Menopause Statement

- Hormone Therapy as First-Line for Vasomotor Symptoms
  - Menopausal hormone therapy (MHT) remains the most effective treatment for hot flashes and night sweats
  - Recommended for healthy women under age 60 or within 10 years of menopause onset, unless contraindicated
  - ACOG stresses lowest effective dose for the shortest duration consistent with treatment goal
- For women who cannot or choose not to use hormones, ACOG supports evidence-based nonhormonal therapies (Same options as NAMS)
  - Lifestyle interventions (exercise, yoga, supplements) are not recommended as sole therapy due to insufficient evidence
- Individualized, Evidence-Based Care
  - Emphasizes personalized treatment plans for menopausal symptom management rather than a one-size-fits-all approach.
  - Decisions should consider age, time since menopause, symptom severity, and patient preferences, along with risk factors for cardiovascular disease, breast cancer, and osteoporosis

# NICE 2024 Update

- Individualized Care and Shared Decision-Making
  - Emphasizes personalized treatment plans and shared decision-making for managing menopause symptoms
  - Stress that HRT should only be prescribed within licensed doses and tailored to age, health status, and preferences
- Hormone Therapy and Cognitive Behavioral Therapy (CBT)
  - HRT remains the most effective treatment for vasomotor symptoms (hot flushes, night sweats)
  - Menopause-specific CBT is now recommended as an adjunct to HRT or as an alternative for those who cannot or choose not to take HRT
    - CBT can also improve sleep and mood and reduce the severity of vasomotor symptoms.
- Genitourinary Syndrome of Menopause (GSM) Management
  - Highlights GSM as a common but often underdiagnosed condition.
  - Recommendations include
    - Offer vaginal estrogen (cream, gel, tablet, pessary, or ring) alone or with systemic HRT
    - Use non-hormonal moisturizers and lubricants when estrogen is contraindicated or declined
    - Shared decision-making is essential for choosing the right formulation

# Case Study Profile

- Name: Tonya
- Age: 54
- Menopausal Status: 3 years post-menopause
- Symptoms: Severe hot flashes, night sweats, vaginal dryness, sleep disturbance
- Medical History: BMI 32 (obese), mild hypertension, no history of breast cancer or VTE
- Labs: Normal lipid profile, bone density shows early osteopenia, history of normal mammograms

# Clinical Considerations

- Individualized Therapy Based on Age and Risk Profile
- Preferred Route
- Regimen
- Alternate options
- Monitoring/Education

# Evidences based Case Study Suggestions

- Individualized Therapy Based on Age and Risk Profile
  - Tonya is within 10 years of menopause onset and under age 60
  - Risk factors: obesity and hypertension which increased VTE risk
- Preferred Route
  - Transdermal estrogen recommended (patch or gel)
    - Bypasses first-pass liver metabolism
    - Reduces impact on clotting factors and lowers VTE risk compared to oral estrogen
- Regimen
  - Start low-dose estradiol patch (0.025–0.05 mg/day)
  - Add oral micronized progesterone 100 mg nightly (uterus intact) for endometrial protection
- Alternative Options (If patient declines hormones)
  - SSRIs/SNRIs or gabapentin
  - CBT for vasomotor symptoms and sleep improvement
- Bioidentical Hormones
  - Educate patient: FDA-approved bioidentical hormones (estradiol, micronized progesterone) are safe.
  - Avoid compounded bioidenticals due to lack of regulation
- Monitoring
  - Follow-up at 3 months for symptom relief and side effects
  - Annual review: BP, weight, breast exam, bone health

# Clinical Take-Aways

- Individualize therapy based on risk and preference
- Combine pharmacologic and lifestyle interventions
- Stay updated with emerging therapies and guidelines

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