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Menopause Matters: Symptoms, Hormones and Genitourinary Health

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Speaker Disclosures

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Overview

1. Understand common symptoms associated with the menopause transition and treatment options
2. Review practice pearls on prescribing menopausal hormone therapy
3. Review diagnosis and management of Genitourinary Syndrome of Menopause (GSM)

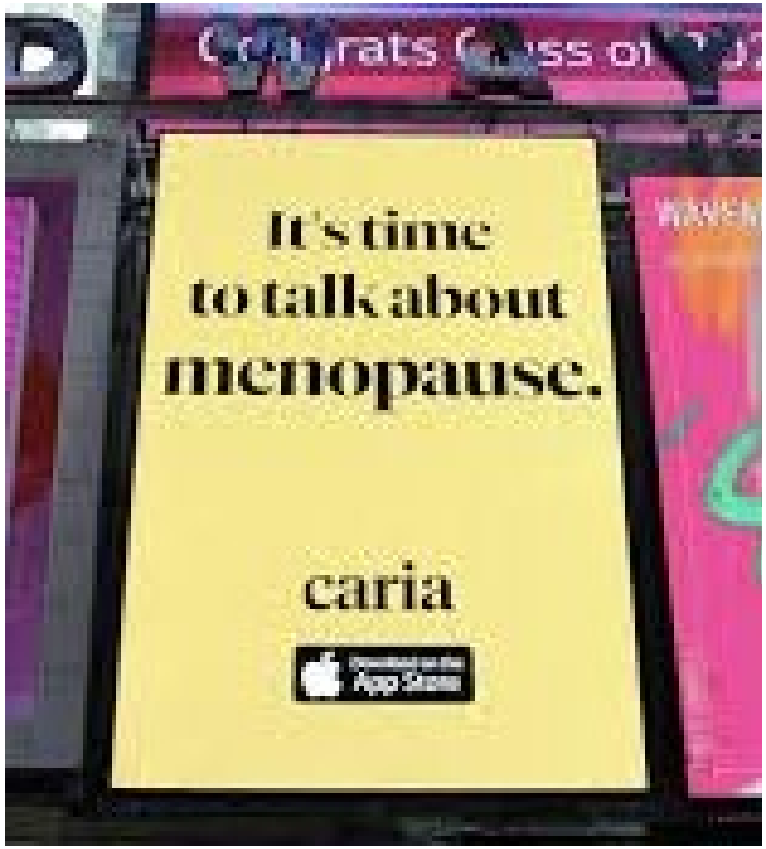
Demographics (US)

- As of 2022, number of women ≥ age 50 estimated to be *64 million*
- ~ 6,000 US women reach menopause every day (over 2 million per year)
- A woman's life expectancy is estimated at *80.2 years*
- US women who survive to age 50 expected to live average of 33.3 more years
  - *60% of women survive until at least age 80*
- ***Women will spend up to 40% of their lives after menopause transition***

Menopause Practice: A Clinician's Guide, 6th ed.
US Census Bureau www.census.gov/data/tables/2022

Menopause in the “mainstream”- Why now?

- Social media, celebrities, Femtech, podcasts
- Telehealth platforms
- Investor interest
- **Media publications:**
  - **NYT article- Feb 1, 2023 *“Women have been misled about menopause”* by Susan Dominus**
- Updated review articles:
  - JAMA May 2024, *WHI Randomized Trial and Clinical Practice: A Review* Manson JE, et al



Menopause

Median age in US women is 51-52 years

- Reached upon 12 consecutive months of amenorrhea
- Age range 40-58 yrs
- < age 40yrs, Primary Ovarian Insufficiency (1%)

Perimenopause: transitional period, median duration 4 yrs

- Fluctuating FSH/estradiol levels, erratic menstrual bleeding
- VMS, mood changes, vaginal symptoms may start
- STRAW : defines stages of the menopause transition[1]

Soules MR et al. Climacteric 2001:267-272

Diagnosis of menopause

- Limited use for FSH/E2 testing in a naturally cycling woman
  - Cyclic bleeding indicates ovarian hormone production
  - FSH and E2 vary at different points in the cycle
  - FSH/E2 levels fluctuate widely during the menopause transition

- Menopause is a *clinical* diagnosis: 12 consecutive months of amenorrhea

- In women < age 45, consider testing TSH, HCG, prolactin if prolonged amenorrhea

- *Special circumstances*: contraception, s/p hysterectomy or endometrial ablation (when menstrual bleeding cannot be assessed)

Vasomotor symptoms (VMS)

- Hot flashes and night sweats: "hallmark" of the menopause transition
- ~75% of women experience VMS during menopause
- Frequency and severity varies among women
- Adverse effects on quality of life[1]
- Primary reason for women to seek treatment during menopause[2]
- Associated with adverse health effects:
  - Depression (perimenopause)[3]
  - Bone health[4]
  - CVD

1. *Avis NE et al Menopause 2009*
2. *Williams RE, et al Maturitas 2007*
3. *Joffe H et al, Menopause 2002*
4. *Crandall CJ, et al. J Bone Mineral Res 2011*

SWAN: Study of Women Across the Nation
Duration of VMS during the menopause transition

- Longitudinal study of 3302 US women (age 42-52 at enrollment) followed for 17 years across the menopause transition
- **Median duration of VMS was 7.4 yrs**
- **Multi-center, diverse ethnic cohort**
  - 5 racial/ethnic groups included (African American, White, Chinese, Hispanic, Japanese)
  - Black women: highest prevalence of VMS, longest total VMS duration (median 10.1 yrs), earlier onset
  - Hispanic women (8.9 yrs), Non-Hispanic white women (6.5 yrs)
  - Japanese/Chinese women: lowest prevalence of VMS, shortest VMS duration (4.8 and 5.4 yrs)
- VMS more prevalent in women with:
  - mood disorders, smoking and low socioeconomic status
- **VMS may start prior to menstrual cycle change**
  - 32% of premenopausal women reported VMS (Lean body mass and VMS study)

Avis et al. JAMA Int Med 2015, Woods et al. Women's Midlife Health 2020

Genitourinary Syndrome of Menopause (GSM)

- More fully describes effects of estrogen loss on genital and urinary symptoms in menopausal women
  - Vulvovaginal atrophy (VVA) is a component of GSM
- Most commonly reported symptoms:
  - Vulvar irritation
  - Inadequate lubrication
  - Burning
  - Dysuria
  - Painful intercourse
  - Vaginal discharge

Severe Vulvar Atrophy

minora atrophied and no longer existent. Fusion of superior l
uring clitoris.

Menopause 2014; 21: 1063-65

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Mood and cognitive changes

- Perimenopausal women more likely to report symptoms of depression and anxiety[1]
- Risk for new onset depression increases in both peri- and postmenopause[2]
- Vasomotor symptoms associated with self-reported depression and anxiety in peri-menopausal women[3]
- Perimenopause may be associated with a slight, *transient* decline in cognitive function[4]

1. Bromberger JT et al. J Affect Disord 2007;103:267-272
2. Bromberger JT, et al. *Obstet Gynecol Clin North Am* 2011;38:609-625
3. Seritan AL et al. *Menopause* 2010;2:410-5
4. Greendale GA et al. *Neurology* 2009;72:1850-1857

Cognitive complaints during menopause

- Frequent in midlife women, negatively affect quality of life
- ~60% report difficulty with memory over the menopause transitions
  - **"Brain fog"** – constellation of cognitive symptoms
    - Memory and attention difficulties
    - Forgetfulness
    - Difficulty with word/number recall
    - Difficulty concentrating
    - Disruption of daily life (e.g. misplacing items)
    - Difficulty switching between tasks
    - Distractability

Maki PM, Jaff MG Climacteric 2022;25(6):570-578

Cognitive complaints during menopause

- Severity of symptoms often in mild range, duration is transient for most women
- *Not* indication of early onset Alzheimer's Disease (rare < age 64)
- Other symptoms may be contributing to cognitive issues during the menopause transition
  - VMS: physiological hot flushes (objectively measured) are associated with decreased verbal memory
  - Depressive symptoms: associated with decreased verbal memory, slower processing speed
  - Sleep difficulties: severity of insomnia associated with worse simple attention in peri but not postmenopausal women

Maki PM et al Menopause 2008;15(5):848-856, Weber MT at al. Climacteric 2021;24:401-07, Rothenberg KG et al. Alzheimer's Dement 2020

Sexual function during menopause

- Sexual dysfunction is prevalent in menopausal women
- **SWAN**: **2009** dyspareunia increases over the menopause transition, desire and arousal decline later in menopause (vs peri-menopause)[1]
- Older studies reported high prevalence of sexual problems in US women
  - National Health and Social Life Survey, 1999
  - 43% of women ages 18-59 reported any sexual problem
- **PRESIDE 2008,** included measure of *distress* in survey
  - 10-15%: any sexual problem (peak age 45-64)
  - 6-12%: low sexual desire
- **WISHeS**: high prevalence of low sexual desire with distress in middle aged women

1. Avis NE et al. Menopause 2009;16:442-52.
2. Lauman EO et al. JAMA 1999
3. Shifren JA, et al. Obstet Gynecol 2008;112:970-8
4. Leiblum SR et al. Menopause 2006;13:46-56

Other complaints/issues during menopause

Musculoskeletal
- "Musculoskeletal Syndrome of Menopause"[1]
  - Joint pain/arthralgia, sarcopenia, bone loss, osteoarthritis

Hair thinning, hair loss

Skin changes: dryness, changes in elasticity

Weight gain, increase in abdominal adiposity

Sleep disturbance (independent of VMS)[2]

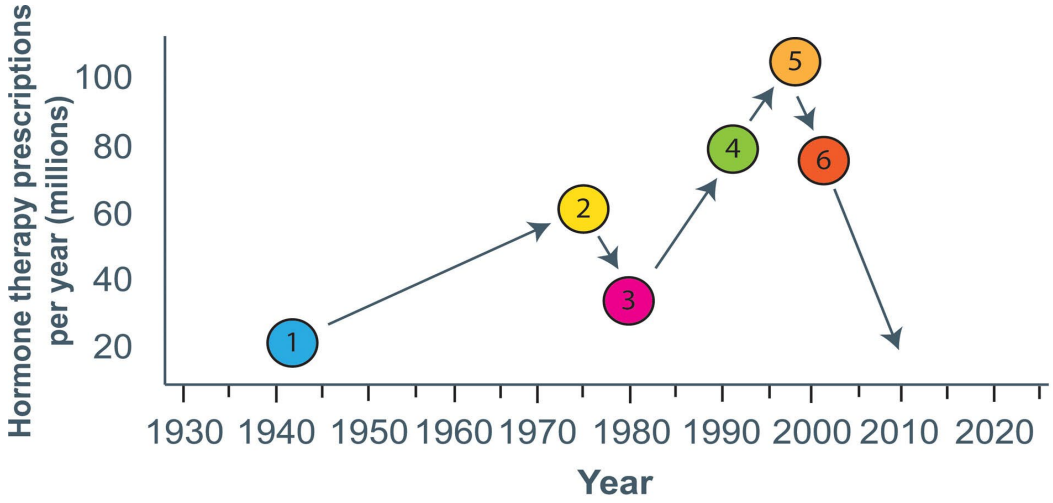
Bone density loss (accelerated loss starts 1yr prior to FMP)[3]

1. Wright et al. Climacteric 2024 2. Matthews et al. Sleep 2021 3. Finkelstein et al. J Clin Endocrinol 2008

Menopausal Hormone Therapy

- **Systemic** estrogen +/- progestin/progesterone highly effective for treatment of menopausal VMS
  - PEPI trial, RCT[1]
    - oral CEE alone and CEE + MPA or progesterone effective
  - Cochrane Review, meta-analysis 24 RCTs[2]
    - 75% reduction in VMS frequency and severity
- 4 FDA approved treatment indications:
  - Moderate-severe menopausal VMS
  - Moderate-severe vulvar and vaginal atrophy due to menopause
  - Prevention of postmenopausal osteoporosis (*exception- estradiol transdermal gel, mist*)
  - Treatment of hypoestrogenism caused by hypogonadism, bilateral oophorectomy, or primary ovarian insufficiency

1. Obstest Gynecol 1998;92:982-988. 2. Cochrane Database of Systematic Reviews 2004: issue 4



Timeline

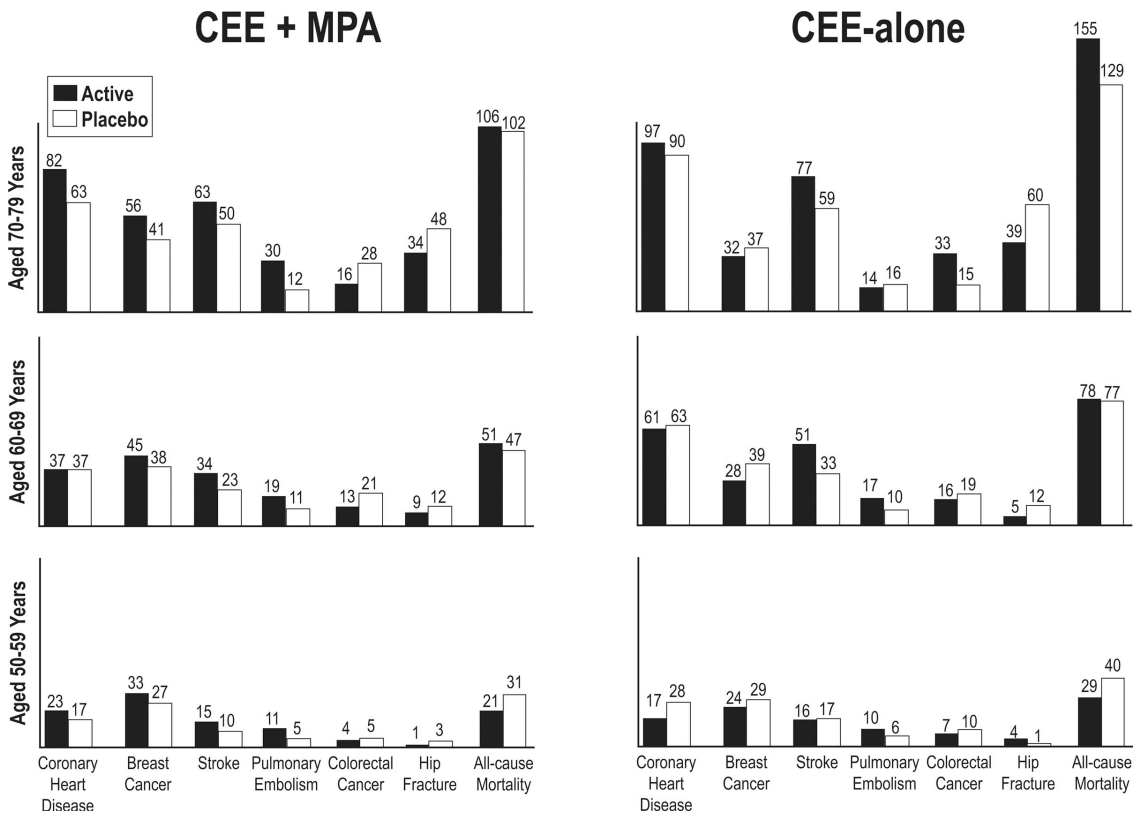
1. 1942: Conjugated equine estrogen first introduced
2. 1975: Endometrial cancer risk recognized
3. 1980: Combined estrogen+progestin introduced
4. 1990s: Nurses' Health Study (1991) + PEPI (1995) published
5. 1998: HERS trial published
6. 2002: WHI trial published

Leslie Cho. Circulation. Rethinking Menopausal Hormone Therapy: For Whom, What, When, and How Long?, Volume: 147, Issue: 7, Pages: 597-610, DOI: (10.1161/CIRCULATIONAHA.122.061559)

What did we learn from the WHI?

- Risks/benefits of a **fixed dose, oral Conjugated Equine Estrogen (CEE 0.625mg) with Medroxyprogesterone Acetate (MPA. 2.5mg)** in women with a uterus
- Risks/benefits of a **fixed dose of oral CEE 0.625mg alone** in women who had hysterectomies
  - CEE alone *decreased* breast cancer risk and breast cancer mortality (18 yr f/u study)
- First RCT of menopausal HT to show reduction in hip and vertebral fracture
- Not a study of menopausal symptom treatment!
- Systemic HT associated with increased risk of dementia in women age 65 and older (WHIMS)
- What not to do….
  - *Initiating* systemic HT in older women (> age 60, > 10 yrs from FMP)– associated with increased CVD, stroke risk

Rossouw JE et al. JAMA 2002, Chlebowski RT et al. JAMA 2020



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Menopause: where we are now?

- **Guidelines do not recommend using HT for chronic disease prevention** *(possible exception: prevention of osteoporosis)*
- **Not starting older women on HT (age 60 and older, > 10 years since menopause)**[1]
  - Timing of initiation" hypothesis- CVD, cognition
    - ELITE trial: 5 yr trial, early < 6 yrs vs late 10 yrs from menopause[2]
    - KEEPS trial: 4 yr trial, initiation within 3 yrs of menopause: neutral effect[3]
- **Safer formulations:**
  - Route of delivery and VTE risk (transdermal vs oral)
  - Type of progestogen: micronized progesterone (MP) vs. medroxyprogesterone acetate (MPA)
    - Breast health, thrombotic risks
  - Type of estrogen: Conjugated estrogen vs 17 estradiol
    - Breast health, thrombotic risks

1. Rossouw JE et al. JAMA 2007 2. Hodis HN et al. NEJM 2016 3. Harman SM et al Ann Intern Med 2014

- "

Menopausal HT: Reducing the risks

- **Transdermal ET** associated with lower risk of venous thromboembolism (VTE) than oral ET (observational studies, No RCTs)
  - Avoidance of first pass hepatic metabolism → absent increase of procoagulant factors
  - Rovinski et al. 2018, meta-analysis
    - VTE risk **oral HT: OR 1.66** (1.39-1.98) vs non-oral OR 0.97 (0.9-1.06)
  - Canonico et al 2008, meta-analysis
    - VTE risk **oral estrogen OR 2.5** (CI 1.9-3.4) vs transdermal 1.2 (0.9-1.7)
  - Mohammed et al 2015
    - VTE risk **oral estrogen OR 1.66** (1.42-1.93) vs transdermal
  - Goldstajn et al. 2023 systematic review, 10 studies identified
    - All studies consistent in reporting transdermal estrogen safer than oral for VTE risk

  Some studies also reported on small elevations in VTE risk with addition of progestin vs progesterone

Black Box Warning

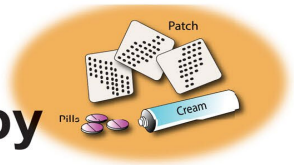
- Added to prescribing information for ALL products containing estradiol or progestogen
- Risks cited were from the WHI (risks for oral CEE 0.625mg/MPA 2.5mg and oral CEE 0.625mg)
- Risks do not apply to low dose (“local”) vaginal estrogen used for GSM
- CVD risks do not account for timing of initiation
- Risks do not apply for all formulations and doses
  - Transdermal, vaginal, micronized progesterone
- **November 2025: FDA announces removal of black box warning !**

Makary M et al. JAMA 2025

Menopausal Hormone Therapy: "Ideal Candidate"

- **Recently menopausal (or peri-menopausal)—"younger"**
  - Within 10 yrs of menopause or age <60
- **Bothersome vasomotor symptoms (benefits > risks)**
- **No absolute contraindications to hormone therapy:**
  - Breast cancer, history of venous thrombosis (deep vein thrombosis, pulmonary embolism)
  - Undiagnosed irregular or postmenopausal bleeding
  - Active liver disease
- **No elevated risk for cardiovascular disease, breast cancer**
  - *10 yr ASCVD risk calculator, Breast cancer risk assessment- Tyrer Cuzick, GAIL*

Menopausal Hormone Therapy



Low Risk HT
- Recent menopause
- Normal weight
- Normal blood pressure
- Physically active
- 10 year ASCVD risk <5%
- Low risk for breast cancer

Intermediate Risk HT
- Diabetes
- Smoking
- HTN
- Obesity
- Sedentary/ Limited mobility
- Autoimmune disease
- Hyperlipidemia
- Metabolic syndrome
- 10 years ASCVD risk ≥ 5 - 10%
- High risk for breast cancer

High Risk HT*
- Congenital heart disease
- ASCVD/CAD/PAD
- Venous thrombosis or pulmonary embolism
- Stroke/TIA or MI
- Breast cancer
- 10 year ASCVD risk ≥10%*

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Estrogen formulations: ORAL

- Conjugated (equine estrogens) 0.3-1.25mg
- Synthetic conjugated estrogens, A 0.3-1.25mg
- Synthetic conjugated estrogens, B 0.3-1.25mg
- Esterified estrogens 0.3- 1.25mg
- 17 β estradiol 0.5-2mg

Estrogen formulations: TRANSDERMAL

Patches: 17 b-estradiol matrix patch

- Once weekly and twice weekly dosing
- Wide range of dosages (0.025, 0.0375, 0.05, 0.06, 0.075, 0.1)
- Very low dose, 0.014 mg/day
  - (approved for osteoporosis prevention only, recent data showing efficacy for hot flashes)

Dermal:

- Gel, spray: 17 b-estradiol
  - *Estradiol gel pump* 0.06%
  - *Estradiol gel packets* 0.1%** (0.25mg, 0.5mg, 1.0mg, 1.25mg)
  - *Estradiol spray (titrate 1-3 actuations/day)*

Estrogen formulations: VAGINAL

Creams

- Conjugated equine estrogen (0.625mg CE/gram)
- Estradiol (100mcg E2/gm)

Tablets/Suppositories

- Estradiol (10 mcg/tablet or 4mcg or 10 mcg insert)

Rings:

- Systemic: Estradiol (silastic ring delivers 0.05mg/day, 0.1mg/day)
- Local: Estradiol (delivers 7.5mcg E2/day)
  - 2mg E2 ring, 90 day dosing interval

Progesterone and Progestins

- Given for endometrial protection only, in women with a uterus
- ***Progesterone (micronized)***
  - Continuous 100-200mg/day
  - Cyclic 200mg/day x 12-14 days monthly
- ***Synthetic progestins***
  - Medroxyprogesterone acetate (MPA) 2.5mg/day, 5mg days 1-12 monthly
  - Norethindrone acetate
  - Drospirenone
  - Levonorgestrel: combination E/P patch, 52mg progestin releasing IUD (off label)

**side effects: breast tenderness, bloating, fluid retention, headaches*

Combination E/P formulations

- **Oral**
  - CEE + MPA
  - CEE + MPA, cyclic
  - Ethinyl estradiol+NETA
  - 17β estradiol + NETA
  - 17 β estradiol +DRSP
  - **Estradiol 1mg+ micronized progesterone 100mg**

MPA medroxyprogesterone acetate

CEE conjugated equine estrogen

NETA norethindrone acetate

DRSP drospirenone

- **Transdermal (patches)**
  - 17 β estradiol + NETA
    - 0.05mg E + 0.14 P
    - 0.05mg E + 0.25mg P
  - 17 β estradiol + levonorgestrel
    - 0.045mg E+ 0.015mg P

FDA-approved "Bioidentical" Hormone Therapy

Active ingredient	Brand (manufacture)[b]	Preparations	Strength	Dosing frequency
17β-estradiol Oral	Estrace (Warner Chilcott, Rockaway, NJ)	Tablet	0.5, 1, or 2 mg	Once daily
17β-estradiol Transdermal	Alora (Watson Pharmaceuticals, Corona, CA)	Patch	0.025, 0.05, 0.075, or 1 mg/d	Twice weekly
	Climara (Bayer HealthCare Pharmaceuticals, Wayne, NJ)	Patch	0.025, 0.0375, 0.05, 0.06, 0.075, or 0.1 mg/d	Once weekly
	Divigel (Upsher-Smith Laboratories, Maple Grove, MN)	Gel (topical)	0.25, 0.5, or 1 mg/packet	Once daily
	Elestrin (BioSante Pharmaceuticals, Lincolnshire, IL)	Gel (topical)	0.87 g/pump	Once daily
	Estrasorb (Novavax, Columbia, MD)	Emulsion (topical)	1.74 g/pouch	Two pouches once daily
	Estrogel (Ascend Therapeutics, Herndon, VA)	Gel (topical)	1.25 g/pump	One pump once daily
	Evamist (VIVUS, Mountain View, CA)	Spray (topical)	1.53 mg/spray	Initially one spray daily; may increase to two to three sprays if needed
	Menostar (Berlex Laboratories, Montville, NJ)	Patch	0.014 mg/d	Once weekly
	Minivelle (Noven Pharmaceuticals, New York, NY)	Patch	0.025, 0.0375, 0.05, 0.075, 0.1 mg/d	Twice weekly
	Vivelle-Dot (Novartis Pharmaceuticals, East Hanover, NJ)	Patch	0.025, 0.0375, 0.05, 0.075, or 0.1 mg/d	Twice weekly
17β-estradiol Vaginal	Estring (Pfizer, New York, NY)	Ring	7.5 mcg/24 h	Once every 90 days
	Femring (Warner Chilcott Laboratories, Rockaway, NJ)[c]	Ring	0.05 or 0.1 mg	Once every 90 days
	Vagifem (Novo Nordisk Pharmaceuticals, Princeton, NJ)	Vaginal Tablet	10 mcg	Once daily for 2 wk, then twice weekly
	Estrace (Warner Chilcott Laboratories, Rockaway, NJ)	Vaginal Cream	0.1 mg/g	Once daily 2-4 g for 1-2 wk followed by 1-2 g for 1-2 wk; 1 g maintenance dose 1-3 times weekly
Progesterone Oral (micronized)	Prometrium (Schering-Plough Research Institute, Kenilworth, NJ; Solvay Pharmaceuticals, Marietta, GA)	Capsules	100 or 200 mg	Once daily
Combined Estradiol and norethindrone acetate[d]	Combipatch (Rhône-Poulenc Rorer, Paris, French)	Patch	0.05/0.14 or 0.05/0.25 mg per day	Twice weekly
Combined Estradiol and levonorgestrel[d]	Climara Pro (Berlex Laboratories, Montville, NJ)	Patch	0.045/0.015 mg per day	Once weekly
Combined Estradiol and norgestimate[d]	Prefest (R.W. Johnson Pharmaceutical Research Institute, Raritan, NJ)	Tablet	1 mg /0 mg ×15 and 1 mg/0.09 mg ×15	Once daily

Conjugated Estrogens/Bazedoxifene (CE/BZD)

- BZD is a Selective Estrogen Receptor Modulator (SERM) or estrogen receptor agonist/antagonist with addition of conjugated estrogen (TSEC, tissue selective estrogen complex) – brand name Duavee
- "Progestin-free" HT option for VMS (BZD is estrogen receptor antagonist in endometrium)
- FDA approved Sept 2013
- CE 0.45mg/20mg Bazedoxifene, once daily oral therapy
- Novel therapy for indication of:
  - treatment of mod-severe hot flashes associated with menopause
  - prevention of postmenopausal osteoporosis
  - *In women with a uterus*

Conjugated Estrogens/Bazedoxifene (CE/BZA)

- 75% reduction in HF frequency vs 50% placebo (by 12 weeks)
- Provides endometrial protection with *higher amenorrhea rates* vs. standard HT
  - (87% CE 0.45mg/BZA 20mg vs. 54% CE 0.45/MPA 1.5mg)
- Lower incidence of breast pain and tenderness
- Does not appear to increase mammographic breast density
- Preliminary evidence that CE/BZD reduces risk biomarkers for postmenopausal breast cancer
- May be good option for women intolerant to progesterone or with breast tenderness
- Similar efficacy for treating hot flashes, preserving BMD across different ethnic groups (non-Hispanic white, African American and Hispanic)[3]

Fertil Steril 2009, Menopause 2016, Cancer Prev Res (Phila) 2019

Treatment Options for VMS

Level 1 -- Good and consistent scientific evidence

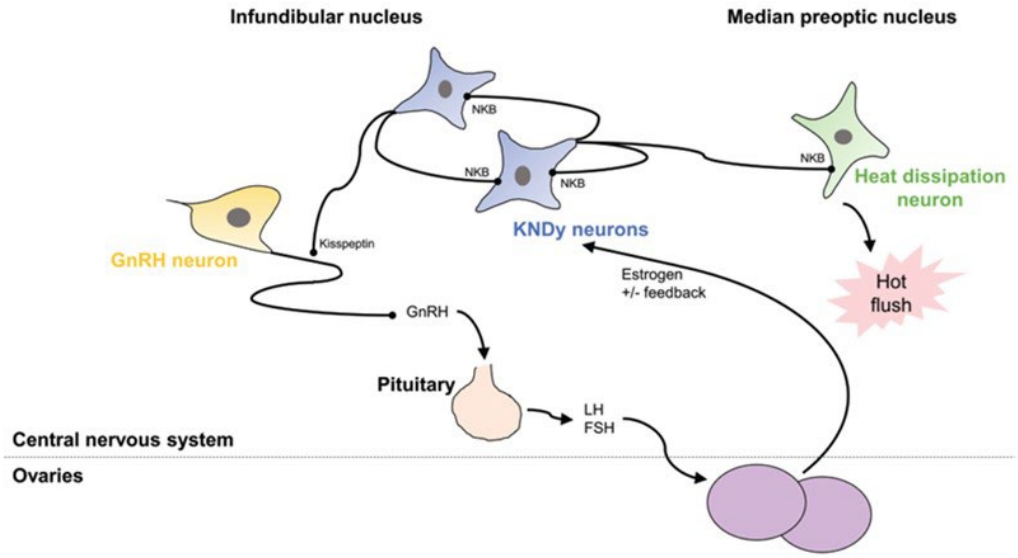
- Hormone Therapy
- SSRI/SNRIs (paroxetine mesylate 7.5mg FDA approved)
- Gabapentin (off label)
- Neurokinin receptor antagonists
- Cognitive behavioral therapy
- Hypnosis

Level 1-2

- Oxybutynin (off label)

- ***Hormone therapy includes:***
  - Estrogen + progestogen (if uterus)
  - Estrogen + bazedoxifene (SERM) (if uterus)
  - Estrogen only (no uterus)
  - Progesterone

Pathophysiology of Vasomotor Symptoms



- Pathophysiology is multifactorial.
- Involves complex interplay between central nervous system and peripheral physiologic processes.
- Kisspeptin-neurokinin B-dynorphin (KNDy) neurons that control the gonadotropin-releasing hormone (GnRH) pulse generator are activated by decreasing estradiol serum concentrations in the menopause transition. This causes an activation cascade to the adjacent thermoregulatory center causing VMS.
- Blockade of neurokinin receptors on KNDy and thermoregulatory neurons reduces or eliminates VMS.
- Small increases in temperature trigger thermoregulatory mechanisms causing the sensation of a hot flush (vasodilation, sweating, and decreased skin resistance) due to a narrowing of the normal thermoregulatory zone.

Reproduced from Santoro N, Roeca C. The menopause transition: signs, symptoms, and management options. *J Clin Endocrinol Metab* 2021;106:1-15; by permission of Oxford University Press on behalf of the Endocrine Society. All rights reserved.

Freedman RR. *Semin Reprod Med* 2005;23:117-125. doi: 10.1055/s-2005-869479; Santoro N, et al. *J Clin Endocrinol Metab* 2021;106:1-15. doi: 10.1210/clinem/dgaa764

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Neurokinin (NK) receptor antagonists

- **Fezolinetant (brand name Veozah): targets NK 3 receptor**
- 45 mg oral pill, once daily
- Contraindications:
  - Known cirrhosis, severe renal impairment or ESRD, concomitant use of CYP1A2 inhibitors
- Precautions: elevated serum transaminases
  - Check baseline LFTs, do not start if >2x upper limit normal or if total bilirubin elevated
  - Repeat transaminases at baseline and monthly x 3 then 6 and 9 months after initiation of therapy
  - Most common adverse reactions: (>2%)
    - abdominal pain (4.3% vs 2%), diarrhea (3.9% vs 2.6%), insomnia (3.9% vs 1.8%),

      hot flush (2.5% vs 1.6%) , hepatic transaminase elevation (2.3% vs 0.8%)

Neurokinin (NK) receptor antagonists

- **Elinzanetant (brand name Lynkuet): targets NK 1 and 3 receptor**
- Two 60mg capsules, once daily
- Contraindications: Pregnancy
- Precautions:
  - CNS depressant effect and impairment
  - elevated serum transaminases: 0.6% vs 0.4%
    - check at baseline, 3 months
  - concomitant use of CYP3A4 inhibitors
  - seizure disorder
  - Most common adverse reactions compared to placebo: ($\geq 5\%$)
    - Headache (9.6% vs 7%), fatigue (7.3% vs 2.9%), dizziness (6.1% vs 1.9%), somnolence (5.1% vs. 1.3%)

GSM- Treatment options

OTC vaginal lubricants and moisturizers

Vaginal estrogen (minimal systemic absorption, no need to oppose with progestin)

- Cream
  - Estradiol 0.01%, conjugated equine estrogen 0.625mg/gm
- Tablet
  - Estradiol 10 mcg, preloaded in applicator, 2x/week
- Insert
  - Estradiol 10 mcg or 4 mcg, no applicator 2x/week
- Ring
  - Estradiol 2mg ring (delivers 7.5mcg estradiol/day), change q3 months

Vaginal DHEA (prasterone 6.5mg, ovule, daily)

Oral SERM (estrogen agonist/antagonist): ospemiphene 60 mg oral tablet daily

Effects of Hormone Therapy on Sexual Function

- Relationship factors and physical and mental health are more important than estrogen levels or menopause status for sexual health.
- Benefits of HT on sexual function may be indirect.
- Improvement in vaginal dryness and dyspareunia can improve pain, hence improve desire.
- Improvement of bothersome hot flashes, night sweats, and related insomnia could improve sense of well-being, and in turn, sexual desire.

Clayton AH, et al. *Mayo Clin Proc* 2018;93:467-487. doi: 10.1016/j.mayocp.2017.11.002; Parish SJ, et al. *Menopause* 2023;30:781-783. doi: 10.1097/GME.0000000000002190; Santoro N, et al. *J Sex Med* 2016;13:305-316. doi: 10.1016/j.jsxm.2015.11.015

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Testosterone therapy in postmenopausal women: is there quality evidence?

- **Testosterone patch 300 mcg for HSDD**
  - Shifren JL et al. 2000
    - RCT 75 women after hysterectomy/BSO on oral estrogen, 150mcg, 300mcg, placebo
    - 300 mcg Treatment group- increase in sexual activity, sexual interest, improvement in well being
  - Buster JE et al. 2005
    - Phase III RCT of 533 women after hysterectomy/BSO, using oral or TD estrogen therapy and 300mcg T transdermal patch, 24 wks
      - Treatment group had more satisfying sexual episodes/month vs placebo, increase in desire, decrease in personal distress, well tolerated, median T levels were above upper limit (wk 12= 73, wk 24=65)
- **Testosterone 300 mcg transdermal daily gel**
  - Safety: no safety signal for CV events or breast cancer
  - Efficacy: in phase III trials, did not meet efficacy endpoint

Testosterone Therapy for Hypoactive Sexual Desire Disorder

- HSDD is not diagnosed on the basis of low serum testosterone; it is a clinical diagnosis.
- Increasing testosterone levels within female physiologic range can improve sexual function in some women (satisfactory sexual event frequency, sexual desire, arousal, orgasm, responsiveness, self-image) and reduces sexual concerns and distress in postmenopausal women.
- Meta-analyses show no severe AEs with physiologic testosterone use.
- Monitoring total testosterone levels and response to treatment is recommended.
- Checking testosterone levels helps to exclude women with high baseline testosterone ranges and prevents androgen excess AEs.
- Long-term safety of testosterone therapy has not been established.

Clayton AH, et al. *Mayo Clin Proc* 2018;93:467-487. doi: 10.1016/j.mayocp.2017.11.002; Davis SR, et al. *Climacteric* 2019;22:429-434. doi: 10.1080/13697137.2019.1637079; Davis SR, et al. *J Sex Med* 2019;16:1331-1337. doi: 10.1210/jc.2019-01603; Islam RM, et al. *Lancet Diabetes Endocrinol* 2019;7:754-766. doi: 10.1016/S2213-8587(19)30189-5; Parish SJ, et al. *Menopause* 2023;30:781-783. doi: 10.1097/GME.0000000000002190

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Testosterone Therapy Dosing (Global Consensus Position Statement)

- Testosterone formulations targeting the normal pre-menopause physiologic range recommended.
- No female testosterone product is currently approved by any national regulatory authority; compounded testosterone preparations are not generally recommended.
- Male formulations can be judiciously used in female doses (1/10), with serum testosterone concentrations monitored regularly.
- Testosterone levels should be checked 6 weeks after initiating and then every 6 months.

Clayton AH, et al. *Mayo Clin Proc* 2018;93:467-487. doi: 10.1016/j.mayocp.2017.11.002; Davis SR, et al. *J Sex Med* 2019;16:1331-1337. doi: 10.1210/jc.2019-01603; Islam RM, et al. *Lancet Diabetes Endocrinol* 2019;7:754-766. doi: 10.1016/S2213-8587(19)30189-5; Parish SJ, et al. *Menopause* 2023;30:781-783. doi: 10.1097/GME.0000000000002190

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Thank you!

- **UCSD Menopause Health Program**
- **Women's Health Services**
  - **La Jolla (VLJ, Genesee)**
  - **Encinitas**
  - **Carmel Valley (PHR)**
  - **Kearny Mesa (Convoy)**
  - **Rancho Bernardo**
  - **Hillcrest (MOS)**