Brigham and Women's Hospital
Founding Member, Mass General Brigham

Clinical Updates and Practical Considerations in Menopause Care

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- Clinical and research foci: Perimenopause and Menopause, Obesity Medicine

Disclosures Summary of Relevant Financial Relationships

I have no relevant financial disclosures.

In compliance with the ACCME, when I discuss specific healthcare products or services, I will use generic names to the extent possible. If I need to use trade names, I will use trade names from several companies when available, and not just trade names from any single company.

I value and respect each individual's gender identity and aim to be inclusive of all patients in need of our care. I recognize the limitations of applying inclusive language when source materials use gender-binary terms and descriptors, and thus I primarily use the terms female and woman when discussing perimenopause, menopause, and the genitourinary syndrome of menopause.

Learning Objectives:

Upon completion of this activity, participants will be able to…

- Identify the significance of menopause as a health risk factor in women and discuss the clinical evaluation of perimenopausal and menopausal patients
- Demonstrate knowledge of the appropriate use of hormone therapy and non-hormone medications in the treatment of perimenopausal and menopausal women
- Discuss the most up to date literature surrounding menopausal hormone therapy

Women Have Been Misled About Menopause

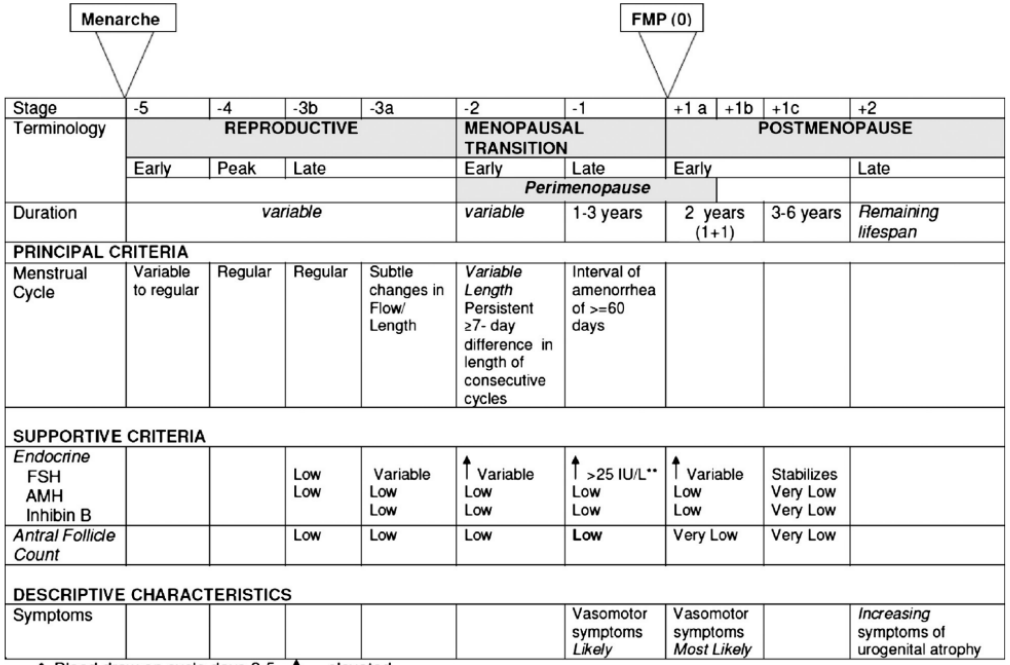
Hot flashes, sleeplessness, pain during sex: For some of menopause's worst symptoms, there's an established treatment. Why aren't more women offered it?

New York Times Magazine: February, 2023

Terminology

- **Natural Menopause:** Cessation of menses for 12 consecutive months after final menstrual period (FMP) due to loss of ovarian follicular activity
  - Early Menopause: < 45 yo
  - Late Menopause: > 55 yo
- **Induced Menopause:** Cessation of menses due to surgical or iatrogenic causes
- **Premature Ovarian Insufficiency (POI):** Menopause occurring < 40 yo

STRAW+10 Classification



Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	variable				variable	1-3 years	2 years (1+1)		3-6 years	Remaining lifespan
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable to regular	Regular	Regular	Subtle changes in Flow/ Length	*Variable Length* Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of >=60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable Low Low	↑ Variable Low Low	↑ >25 IU/L** Low Low	↑ Variable Low Low		Stabilizes Very Low Very Low	
Antral Follicle Count			Low	Low	Low	**Low**	Very Low		Very Low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms *Likely*	Vasomotor symptoms *Most Likely*			*Increasing* symptoms of urogenital atrophy

* Blood draw on cycle days 2-5 ↑ = elevated

**Approximate expected level based on assays using current international pituitary standard[67-69]

FIG. 2. The Stages of Reproductive Aging Workshop + 10 staging system for reproductive aging in women.

Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, Sherman S, Sluss PM, de Villiers TJ; STRAW+10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop +10: addressing the unfinished agenda of staging reproductive aging. Climacteric. 2012 Apr;15(2):105-14.

The Importance of Identifying Age at Menopause in Women

- Age at menopause is a significant marker of health in midlife women
  - Early menopause is associated with increased all-cause mortality and increased risk of cardiovascular disease (CVD), osteoporosis, and dementia
    - Given the established accelerating CVD risk in women undergoing the Menopausal Transition (MT), there is a key role for clinicians to monitor and intervene on the cardiovascular health of their patients that is often overlooked
  - Late menopause may increase risk for breast, endometrial, and ovarian cancer
    - Late menopause has also been associated with increased longevity of life

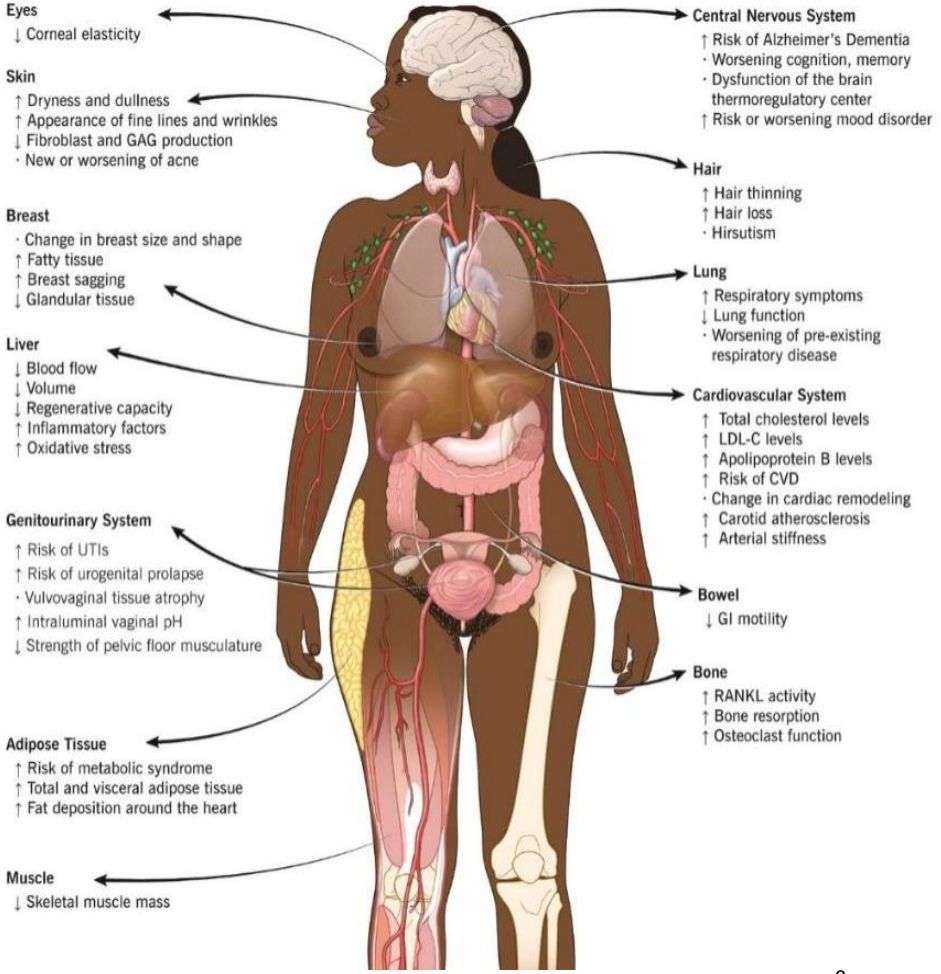
Cardiometabolic Changes During the Menopausal Transition Independent of Aging

- Increased carotid atherosclerosis and arterial stiffness
- Adverse changes in body composition
  - Increased total and visceral adipose tissue
- Increased prevalence of metabolic syndrome
  - Worsening progression during perimenopause
- Worsening lipid profile
  - Increased total cholesterol
  - Increased LDL-C
  - Increased Apolipoprotein B

El Khoudary SR, Aggarwal B, Beckie TM, et al. American Heart Association Prevention Science Committee of the Council on Epidemiology and Prevention; and Council on Cardiovascular and Stroke Nursing. Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association. Circulation. 2020 Dec 22;142(25):e506-e532.

Perimenopausal and Menopausal Symptoms

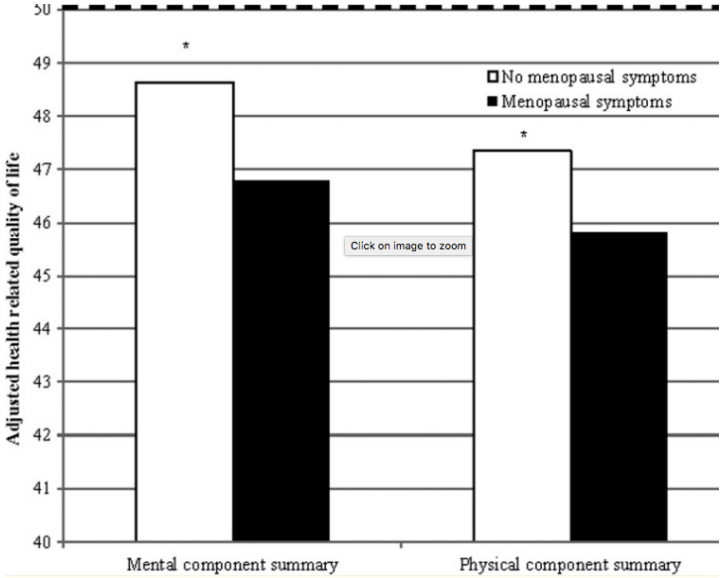
- Estrogen affects every organ system in the body leading to a vast possible symptom profile
- Classic symptoms
  - Change in bleeding patterns, vasomotor symptoms (VMS), genitourinary syndrome of menopause (GSM)
- Other symptoms associated with menopause
  - Sleep disturbances
  - Cognitive concerns (brain fog, memory, concentration)
  - Psychological symptoms
  - Changes to skin and hair
  - Joint pain
  - Weight gain (esp. visceral distribution)
  - Headaches
  - Bone loss



Iyer TK, Thacker HL. "Menopause" In: Falcone T, Hurd WW. Editors. Clinical Reproductive Medicine and Surgery: A Practical Guide, 4th Edition Springer Nature; 2022.

Psychosocial and Economic Considerations

- 2023 Study out of Mayo Clinic estimated $1.8 billion in lost work time per year, and $26.6 billion annually when medical expenses are added, in the U.S. alone
- 2005 United States National Health and Wellness Survey: menopause may cause significant "humanistic and economic burden"
  - Lower mental and physical health-related quality of life (QOL)
  - Symptomatic women experience significantly higher overall work impairment, impairment in daily activities, and more physician visits
- Personal and global financial impact
- Possible relationship issues
- Impact on sexuality
- Impact on physical appearance/confidence



Faubion SS, Enders F, Hedges MS, Chaudhry R, Kling JM, Shufelt CL, Saadedine M, Mara K, Griffin JM, Kapoor E. Impact of menopause symptoms on women in the workplace. InMayo Clinic Proceedings 2023 Jun 1 (Vol. 98, No. 6, pp. 833-845). Elsevier.

Whiteley J, DiBonaventura Md, Wagner JS, Alvir J, Shah S. The impact of menopausal symptoms on quality of life, productivity, and economic outcomes. J Womens Health (Larchmt). 2013 Nov;22(11):983-90. doi: 10.1089/jwh.2012.3719. Epub 2013 Oct 1. PMID: 24083674; PMCID: PMC3820128.

Evaluation: Perimenopause is a Clinical Diagnosis!

- Clinical diagnosis
  - Perimenopause vs Menopause
- Utility of labs
  - FSH
  - 17-B-Estradiol
  - Total testosterone
  - TSH
  - Lipid panel
  - CMP
  - 25-hydroxy vitamin D
- Special considerations
  - Hysterectomy, endometrial ablation
  - Certain forms of contraception
  - Underlying menstrual disorders

Summary of hormones of reproductive aging by STRAW criteria

	Peak Reproductive	Late Reproductive	Early MT	Late MT		Postmenopause
FSH	Normal	↑	↑	↑		↑
AMH	Normal/↓	↓	↓	Undetectable	**FMP**	Undetectable
Inhibin B	Normal	↓	↓	Undetectable		Undetectable
Estradiol	Normal	Normal	Normal	↓		↓

Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, Sherman S, Sluss PM, de Villiers TJ; STRAW+10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop +10: addressing the unfinished agenda of staging reproductive aging. Climacteric. 2012 Apr;15(2):105-14.

CASE #1

52 yo woman presenting with hot flashes, night sweats, mood swings, sleep disturbance, hair thinning and joint pain. It has been 14 months since her last menstrual period.

- PMHx: hypertension, overweight (BMI 29.7), hypothyroidism
- PSHx: none
- Medications: losartan, levothyroxine

What therapy is most effective to treat her symptoms?

Image from: https://www.health.harvard.edu/blog/menopause-related-hot-flashes-night-sweats-can-last-years-201502237745

Management of perimenopausal and menopausal symptoms

- Gold standard of treatment: menopausal hormone therapy (MHT)
- FDA-approved for:
  - Vasomotor symptoms
  - Genitourinary syndrome of menopause
  - Prevention of bone loss/ fracture reduction in postmenopausal women
  - Mitigation of early estrogen loss in surgical menopause/ POI

Image from: https://news.cancerconnect.com/treatment-care/hormonal-therapy

Prescribing Hormone Therapy

- Hormone Therapy: FDA-approved for the treatment of menopausal symptoms
  - **Estrogen alone** – unopposed estrogen for women who are s/p hysterectomy; or can be used locally for GSM
  - **Estrogen + Progestogen** – for women with intact uterus to protect endometrial lining
    - Reasons to consider progestogen use in hysterectomized women
      - History of endometriosis with concern for remnant endometrial tissue
      - For significant falling asleep issues/nighttime anxiety issues
  - **Bioidentical HT** – chemically identical to those made in the body
    - Unregulated – unapproved and untested from various compounding pharmacies
    - Regulated – FDA approved and tested
- Important counseling points: route/dosing, duration of therapy, side effects, risks/benefits

Dosage Ranges

- Dosage ranges typically used with systemic ET
  - 0.014 –0.1 mg Transdermal (TD) 17B- estradiol (dosed weekly or twice weekly—q 3.5 days)
  - 0.5-2 mg oral micronized 17B-estradiol (dosed BID)
  - 0.3-1.25 mg oral conjugated equine estrogen (CEE)
- Typical dose range of progestogen
  - 100-200 mg oral micronized progesterone
  - 52 mg levonorgestrel intrauterine device (IUD)
  - 1.5-5 mg oral medroxyprogesterone acetate (MPA)
  - 0.1-0.5 mg oral norethindrone acetate (NETA)
  - 0.5-2 mg oral drospirenone

CASE #1 continued…

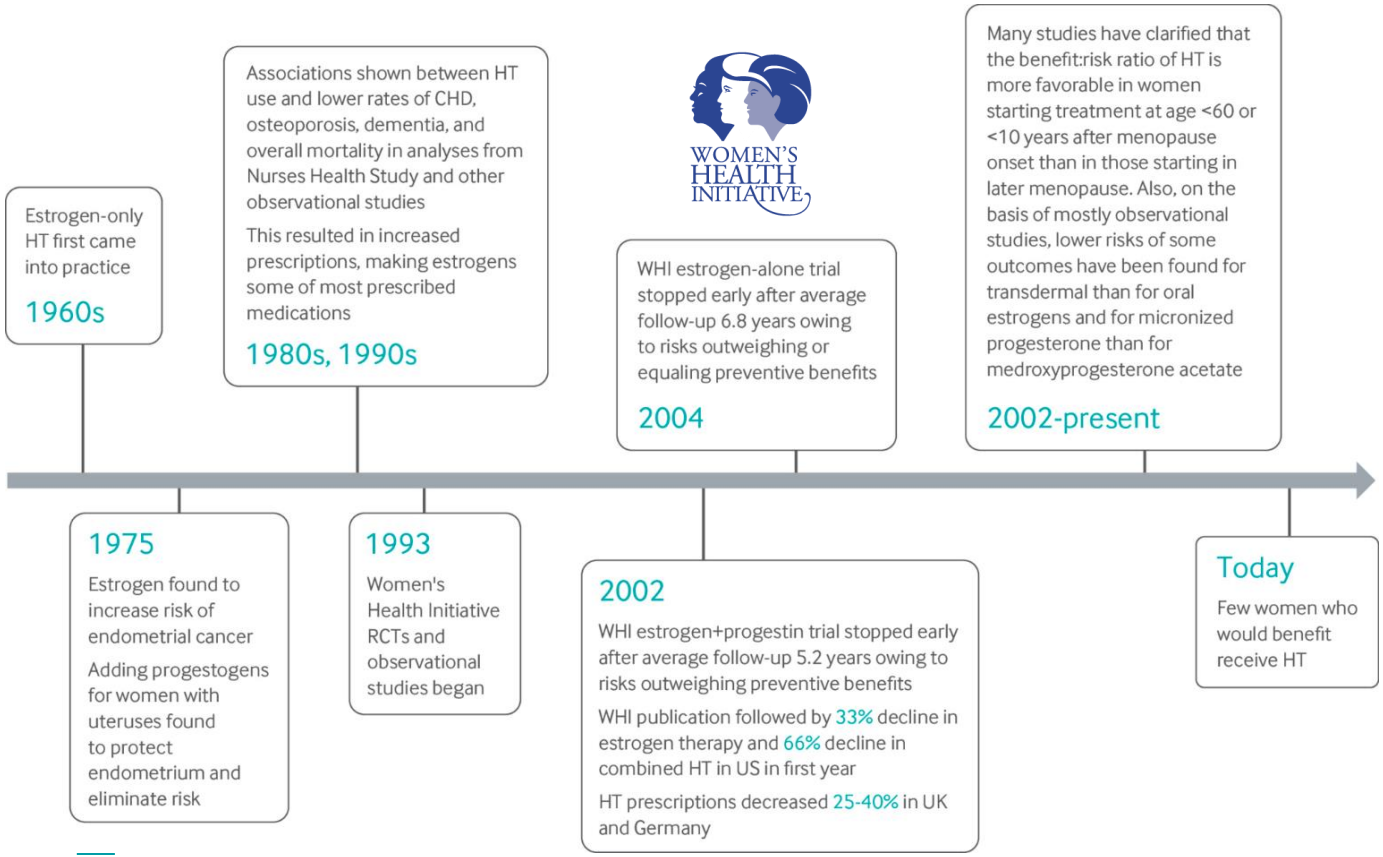
You recommend menopausal hormone therapy for this patient.

She is weary of taking hormones, reporting she has heard they can cause breast cancer and other health problems. She is also worried about side effects.

How would you counsel this patient?

Image from: https://www.health.harvard.edu/blog/menopause-related-hot-flashes-night-sweats-can-last-years-201502237745

The Controversy over Hormone Therapy Explained: A Timeline



Long term benefits of MHT

- Reduction in all-cause mortality (including cancer and stroke mortality)
- Reduction in CVD incidence and mortality
- Reduction in risk of osteoporosis and osteoporotic fractures at the hip and the spine
- Reduction in incidence of colon cancer

Duralde ER, Sobel TH, Manson JE. Management of perimenopausal and menopausal symptoms. bmj. 2023 Aug 8;382.

The Timing Hypothesis

When initiated under the age of 60 years old or within 10 years from menopause in otherwise healthy women, hormone therapy demonstrates greater benefits than risks, especially with respect to cardiovascular disease outcomes.

What Do We Know Today? Breast Cancer Data

- Evidence from the WHI:
  - The risk of breast cancer (BC) related to HT use is rare (less than one additional case per 1,000 women per year of HT use or three additional cases per 1,000 women when used for 5 years with CEE+MPA)
  - No increased risk of breast cancer **mortality**
  - CEE-only users experienced a reduction in breast cancer incidence and mortality compared to controls
- High risk patients:
  - Data does not show an additive effect of HT use and underlying BC risk on BC incidence
  - Observational evidence suggests that HT use does not further increase risk of breast cancer in women at high risk because of a family history or after bilateral salpingo-oophorectomy (BSO) for BRCA 1/2
- Women should be counseled about the risk of breast cancer with hormone therapy, putting the data into perspective, with risk similar to that of modifiable risk factors (i.e. alcohol consumption, obesity, smoking, first child after 30 yo etc.)

Faubion SS, Crandall CJ, Davis L, El Khoudary SR, Hodis HN, Lobo RA, Maki PM, Manson JE, Pinkerton JV, Santoro NF, Shifren JL. The 2022 hormone therapy position statement of The North American Menopause Society. Menopause. 2022 Jul 1;29(7):767-94.

'Tis but a scratch: a critical review of the Women's Health Initiative evidence associating menopausal hormone therapy with the risk of breast cancer

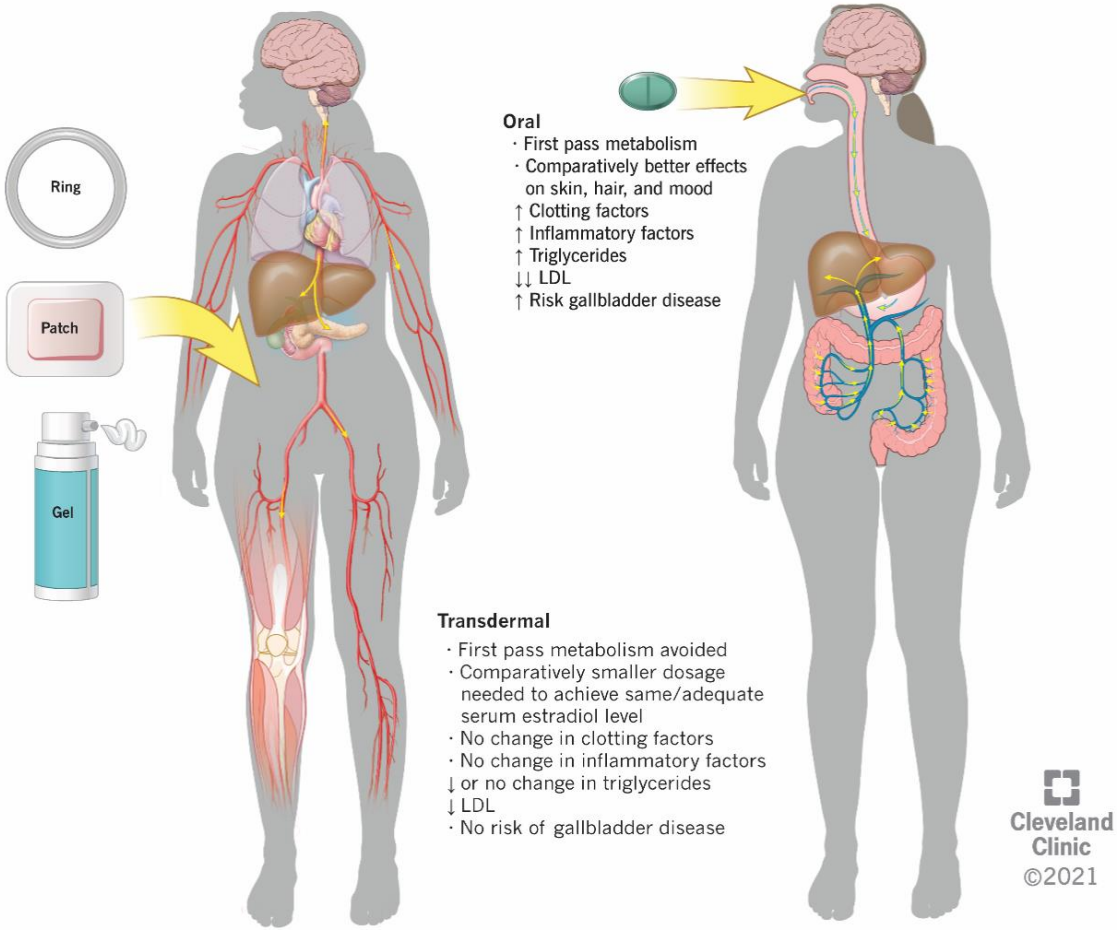
"In sum, findings generated by the WHI to date warrant the following conclusions:

1. *CEE alone significantly reduces breast cancer risk and breast cancer mortality.*
2. *CEE+MPA, when initiated in HT naïve women, does not increase breast cancer risk and does not increase breast cancer mortality, even for women with a family history of breast cancer.*
3. *Even if the WHI estimate of an increased risk of breast cancer is accepted based on the elevated HR, a result driven solely by a low incidence of breast cancer in the placebo group, CEE+MPA would be responsible for less than 1 additional nonfatal breast cancer diagnosis for every 1,000 women treated.*
4. *No estimate of an association between CEE+MPA and breast cancer remains statistically significant with per-protocol adjustment."*

Bluming AZ, Hodis HN, Langer RD. 'Tis but a scratch: a critical review of the Women's Health Initiative evidence associating menopausal hormone therapy with the risk of breast cancer. Menopause. 2023 Apr 4:10-97.

VTE/Stroke risk: TD vs Oral MHT

- Large two nested case control study 2019: Transdermal HT was NOT associated with any increased risk of VTE and consistent among various regimens
- Transdermal HT has not been associated with VTE/stroke risk in multiple observational studies, limited observational data and a systematic review suggest less risk with transdermal HT than oral



Iyer TK, Thacker HL. "Menopause" In: Falcone T, Hurd WW. Editors. Clinical Reproductive Medicine and Surgery: A Practical Guide, 4th Edition Springer Nature; 2022.

Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases. bmj. 2019 Jan 9;364.

Menopausal Hormone Therapy, Mood, and Sleep

- Depression
  - Some evidence that ET has similar efficacy to antidepressants in depressed perimenopausal women with or without VMS and enhances mood and well-being in non-depressed perimenopausal women
  - HT may prevent onset of depressive symptoms in euthymic perimenopausal women and may positively augment clinical response to antidepressants in perimenopausal and postmenopausal women
- Sleep disturbances
  - Sleep disturbances → negative impact of sleep disruption on QOL, mood, memory, metabolic syndrome, obesity, and CV risk
  - Some evidence that TD ET may benefit sleep of perimenopausal women independent of VMS

Faubion SS, Crandall CJ, Davis L, El Khoudary SR, Hodis HN, Lobo RA, Maki PM, Manson JE, Pinkerton JV, Santoro NF, Shifren JL. The 2022 hormone therapy position statement of The North American Menopause Society. Menopause. 2022 Jul 1;29(7):767-94.
Image from: https://www.everydayhealth.com/menopause/women-have-a-harder-time-sleeping-after-menopause/

Menopausal Hormone Therapy, Cognition, and Dementia

- The effect of hormone therapy may be modified by baseline cognitive function, with more favorable effects in women with normal cognitive function before hormone therapy initiation
- HRT may have cognitive benefits when initiated immediately after TAH/BSO in surgical menopause patients
- HT in the early natural postmenopausal period has likely neutral or positive effects on cognitive function, but detrimental effects when initiated after age 65
    - Data is mixed, though most observational data points to a reduced risk of AD when HT is initiated in early menopause
    - Risk of dementia was increased in women who started hormone therapy at age 65 or later in the WHI trials, however, hormone therapy use was not associated with increased mortality from Alzheimer's disease or dementia at 18 year follow-up

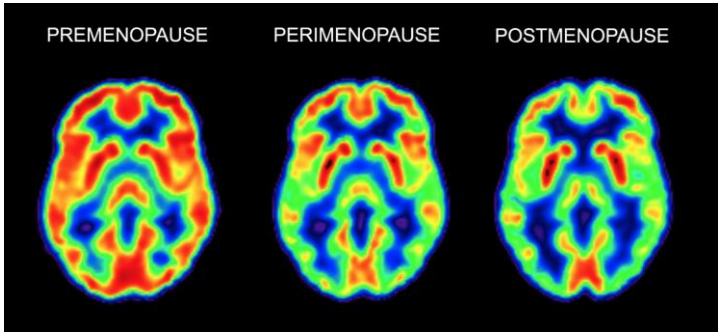


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Image from: https://www.wsj.com/articles/the-link-between-menopause-and-alzheimers-11550509201.

Metabolic Considerations of Hormone Therapy

- Diabetes and Metabolic Syndrome
  - Surgical Menopause (bilateral oophorectomy) is associated with 57% increased risk of T2DM compared to natural menopause
  - MHT is associated with decreased insulin resistance, incidence of diabetes, and lower fasting glucose/insulin levels
  - The menopause transition is associated with increased total and visceral adiposity and decreased lean muscle mass, which can be somewhat mitigated by the use of MHT
  - MHT is neither approved nor appropriate for prevention of T2DM, but it should not be withheld from women at high risk for DM who need MHT for symptom control

Mauvais-Jarvis F, Manson JE, Stevenson JC, Fonseca VA. Menopausal Hormone Therapy and Type 2 Diabetes Prevention: Evidence, Mechanisms, and Clinical Implications. Endocr Rev. 2017 Jun 1;38(3):173-188. doi: 10.1210/er.2016-1146.

Relative Contraindications to HT: Updates from the Menopause Society 2022 Hormone Therapy Position Statement

Severe active liver disease
History of endometrial cancer
History of estrogen-sensitive malignancy
Porphyria Cutanea Tarda
History of deep vein thrombosis
History of pulmonary embolism
History of stroke
~~**Dementia**~~
~~**Hypertriglyceridemia**~~
Coronary Heart Disease
Unexplained vaginal bleeding that has not been evaluated

Removal of statement "...concern that endometriosis might reactivate, migraine headaches may worsen, or leiomyomas may grow"

Faubion SS, Crandall CJ, Davis L, El Khoudary SR, Hodis HN, Lobo RA, Maki PM, Manson JE, Pinkerton JV, Santoro NF, Shifren JL. The 2022 hormone therapy position statement of The North American Menopause Society. Menopause. 2022 Jul 1;29(7):767-94.

Counseling on Side Effects

- Abnormal uterine bleeding can be common in the first 3 months and can even occur up to 1 year
  - Can be due to an estrogen-progestogen imbalance
  - If despite making medication changes bleeding persists, must evaluate the endometrium (transvaginal US +/- endometrial biopsy)

Table 15. Potential Adverse Events of Estrogen Therapy or Estrogen-Progestogen Therapy

- Uterine bleeding (starting or returning)
- Breast tenderness (sometimes enlargement)
- Nausea
- Abdominal bloating
- Fluid retention in extremities
- Changes in the shape of the cornea (sometimes leading to contact lens intolerance)
- Headache (sometimes migraine)
- Dizziness
- Mood changes with EPT, particularly with progestin
- Angioedema
- Gallstones, pancreatitis

Abbreviations: EPT, estrogen-progestogen therapy; ET, estrogen therapy

The North American Menopause Society. Menopause Practice: A Clinician's Guide, 6th ed. 2019.

Duration of Use for Systemic Hormone Therapy

- Hormone replacement therapy is gold standard of care in patients < 45 years old to mitigate deleterious effects of early estrogen loss and should be continued at least until the average age of menopause (~52 years old)
- Per Menopause Society Guidelines, hormone therapy does not need to be routinely discontinued in women aged older than 60 or 65 years
- Longer durations or extended use beyond age 65 years should be considered with periodic reevaluation (at minimum annually) considering severity of symptoms, comorbid conditions, periodic trials of lowering or discontinuing hormone therapy, effectiveness of alternative nonhormone interventions, patient preferences and response to hormone therapy, and underlying risk for osteoporosis, CHD, cerebrovascular accident, VTE, and breast cancer
- As women age, it is recommended to consider risk mitigation using lowest effective dose, nonoral therapy

Faubion SS, Crandall CJ, Davis L, El Khoudary SR, Hodis HN, Lobo RA, Maki PM, Manson JE, Pinkerton JV, Santoro NF, Shifren JL. The 2022 hormone therapy position statement of The North American Menopause Society. Menopause. 2022 Jul 1;29(7):767-94.

CASE #2

48 yo postmenopausal woman with a history of ER+/PR+/HER2- breast cancer currently being treated with tamoxifen with presenting with hot flashes, night sweats, increasing anxiety, weight gain, depressive symptoms, fatigue, and diffuse arthralgias.

She reports she went through menopause at age 47, and only had mild symptoms, but now after starting tamoxifen it feels like her previous symptoms have “returned, but in full force.”

What therapies may be options for her?

Image from: https://www.morelandobgyn.com/blog/perimenopause-symptoms-relief-how-to-find-a-perimenopause-doctor

Non-Hormonal Treatment Options of Menopausal Symptoms

- Antidepressants
  - SSRIs: fluoxetine, escitalopram, citalopram, **paroxetine** (10 mg is lowest generic) → start at the lowest possible dose
    - Only FDA-approved medication is Brisdelle (paroxetine 7.5mg)
    - Paroxetine and fluoxetine are potent CYP2D6 inhibitors → significantly reduce the efficacy of tamoxifen
  - SNRIs: desvenlafaxine (50 mg), **venlafaxine** (37.5-75 mg), duloxetine (30-60 mg)
- Anticonvulsant
  - **Gabapentin**: Starting dose 100-300 mg nightly
    - Can titrate up to 900 mg
- Antihypertensive
  - Clonidine: starting dose 0.1 mg twice a day
- Antispasmodic
  - Oxybutynin: starting dose 2.5-5 mg twice a day, can titrate up to 15 mg

New Developments: NK3R and NK1/3R antagonists

- The thermoregulatory center in the hypothalamus is stimulated by neurokinin 3 receptor (NK3R) activation and inhibited by estrogen-negative feedback
  - This balance is disrupted in menopause, producing vasomotor symptoms
- Fezolinetant: VEOZAH approved by FDA 5/2023
  - SKYLIGHT → Fezolinetant 45 mg was efficacious for the treatment of moderate-to-severe VMS associated with menopause
  - Caution with certain medications (CYP1A2 inhibitors, including caffeine)
  - Need to check liver function tests at baseline, 3, 6, and 9 months
  - Most common side effect: headache, GI disturbances
- Elinzanetant: currently in Phase 3 trials “OASIS” trial
  - OASIS → Elizanetant is a dual NK1/NK3 receptor antagonist being studied for the treatment of vasomotor symptoms

Lederman, Samuel MD; Shapiro CM, Marla MD; Stute, Petra MD; Lee, Misun PhD; Wang, Xuegong PhD; Neal-Perry, Genevieve PhD. Phase 3 Study of Fezolinetant for Treatment of Moderate-to-Severe Vasomotor Symptoms Associated With Menopause [A132]. Obstetrics & Gynecology: May 2022 - Volume 139 - Issue - p 39S doi: 10.1097/01.AOG.0000825808.38519.3b

Evidence-Based Non-Prescription Therapies

- Weight loss
- Mind-body techniques
  - Cognitive behavioral therapy (CBT) → literature demonstrates slight reduction in VMS symptoms and benefits in mood, QOL, and overall functioning
  - Clinical hypnosis → RCTs demonstrated it to be effective in reducing VMS in survivors of breast cancer and in postmenopausal women
- Inconclusive or lack of robust evidence: yoga, acupuncture, s-equol, paced respiration, OTC/herbal supplements (including black cohosh)

The North American Menopause Society. Menopause Practice: A Clinician's Guide, 6th ed. 2019, p 49-51.

CASE #3

A 48 year old woman presents for an annual exam.

She reports her periods have become irregular. Her LMP was 15 days ago and her period was very heavy lasting 9 days. Prior to this month she had not had a period in 2 months. She also endorses intermittent hot flashes/night sweats, sleep changes, and recent weight gain despite no changes to her diet or exercise regimen.

PMHx: Brief hx of tobacco use as a teenager, but has not smoked since she was 19

PSHx: none

Contraception: Husband with vasectomy

What therapies may be options for her?

Image from: https://atriumhealth.org/dailydose/2020/03/09/every-woman-goes-through-menopause-at-some-point-know-how-to-manage

Perimenopause

- Combined hormonal contraception
  - Consider PMHx, safety, symptoms
  - Do they need contraception? Do they have heavy bleeding?
  - Do they have PMDD or menstrual migraines (with or without aura)?
  - Do they have ovulatory or hyperestrogenic symptoms?
- Micronized progesterone with or without transdermal ET
  - Prometrium 200 mg days 1-12 of each calendar month or 100 mg daily
    - May bleed on day 8-10 or after
    - Take at night, it is relaxing and can help sleep
    - Still need to consider contraception
    - Micronized in peanut oil so cannot be allergic to peanuts
    - Micronized progesterone, especially the higher doses, can also reduce hot flashes
- Mirena IUD with or without transdermal ET
  - Great option for endometrial protection, HMB, and contraception

CASE #4

A 72 year old woman presents to for an annual exam.

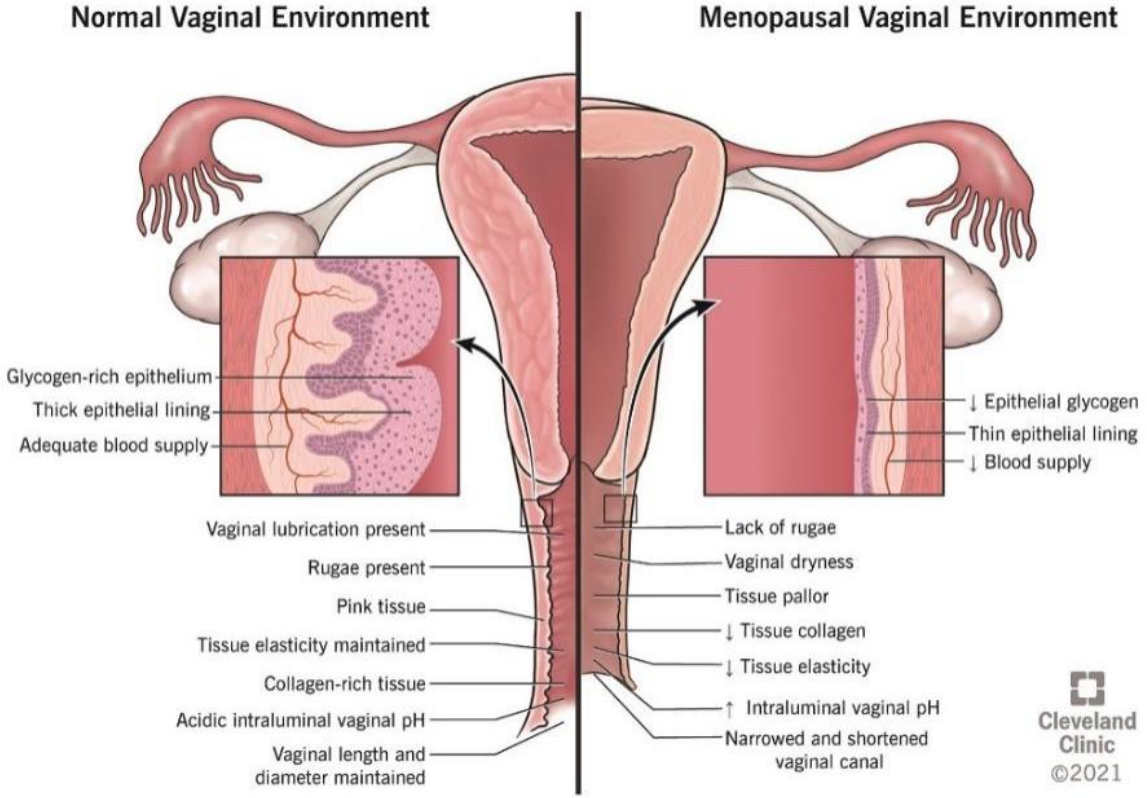
LMP: age 50, no further episodes of bleeding, but having persistent vaginal dryness and discomfort, dyspareunia, and some urinary leakage issues

Genitourinary exam demonstrates frank vulvovaginal atrophy

Image from: https://www.forbes.com/sites/debgordon/2021/07/13/73-of-women-dont-treat-their-menopause-symptoms-new-survey-shows/?sh=42774104454f

Genitourinary Syndrome of Menopause

Labial atrophy
Vaginal dryness
Introital stenosis
Clitoral atrophy
Phimosis of the prepuce
Reduces mons pubis and labia majora bulk
Reduced labia minora tissue and pigmentation
Prominence and erythema of the urethral meatus
Urethral caruncle
Vaginal pallor
Lack of vaginal rugae



Iyer TK, Thacker HL. "Menopause" In: Falcone T, Hurd WW. Editors. Clinical Reproductive Medicine and Surgery: A Practical Guide, 4th Edition Springer Nature; 2022.

GSM: practical considerations for prescribers

- Estradiol Vaginal Ring
  - Vaginal ring (Insert just like nuvaring)
  - One ring q every 3 months
  - Great for patients with incontinence as gives some bladder lift and patients with arthritis/obesity/chronic back pain – where frequent application may be difficult
- Conjugated Estrogen Vaginal Cream
  - Insert via applicator (fill applicator tube with cream then insert) or can use finger to apply to lower 1/3 of vagina
  - Likely only get 1 applicator so need to wash after every use with unscented soap and water
  - Use nightly x 2 weeks then 2-3x/week for maintenance
- Estradiol Vaginal Cream
  - Insertion similar to PVC
  - Use nightly 2 g/d x 2 weeks then 1g 2-3x/week
- Estradiol Vaginal Pearls
  - Suppository of estradiol and coconut oil that looks like elongated pearl
  - Less messy than creams because oil is a good bioadhesive
  - Insert into vagina up to knuckles length
  - Nightly x 2-3 weeks then 2x/week for maintenance
- Estradiol Vaginal Suppositories
  - Estradiol inserts placed with an applicator -> insert to knuckle length
  - Nightly x 2 weeks then 2x/week for maintenance
- Vaginal DHEA
  - Precursor hormone to both estrogens and androgens -> may lead to improved sexual and urinary outcomes
  - Stored at room temp or refrigerated
  - Brand name: Intrarosa 6.5 mg vaginal inserts nightly
  - Compounded option: Vaginal DHEA 13 mg suppository
    - Insert vaginally daily x 1 month then M/W/F or as needed
- Osempifene
  - FDA-approved for moderate to severe dyspareunia secondary to VVA
  - Oral tablet 60 mg take daily with food
  - SERM with estrogenic effects on vaginal mucosa and bone, no endometrial effects
- Fractional CO2 Vaginal Laser Therapy
  - Requires multiple sessions
  - Typically not covered by insurance
  - Recent double-blind, randomized, sham-controlled trial by Fiona et al. 2021 did not show significant improvement with fractional carbon dioxide laser vs sham treatment after 12 months
- Non-prescription therapy: regular sexual activity, lubricants, moisturizers

Key Take Home Points

- Age at menopause is a significant health indicator and an independent risk factor for cardiovascular disease
- HT is the gold standard of treatment for menopausal symptoms in healthy women aged younger than 60 years or within 10 years of menopause onset with no contraindications
    - Absolute risks for HT use in healthy women after 50-59 are rare but can include VTE, stroke, breast cancer
    - Evidence demonstrates improved bone health, cognition, GSM, QOL, CVD risk, all-cause mortality
    - Risks of hormone therapy differ for women, depending on type, dose, duration of use, route of administration, timing of initiation, and whether a progestogen is needed → consider each patient's own risks prior to starting HT
- There are effective non-hormonal options for the treatment of vasomotor symptoms for patients with contraindications or who cannot tolerate or do not want HT
- GSM should be assessed in all postmenopausal women and treated accordingly with one of several effective, safe therapeutic options
- Treatment of menopausal symptoms should be individualized using the best available evidence to maximize benefits and minimize risks, with periodic reevaluation

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Questions?

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