# Menopause: 10 Tips

Moira K. Ray, MD MPH
Associate Professor of Family Medicine, OHSU

Many thanks to Karen Adams, Amanda Clark, Craig Williams and the Oregon ECHO team

# Conflicts

• I have received compensation from the Oregon ECHO network to teach on menopause in the past year

# Objectives

- Contextualize historical menopause research on current knowledge & gaps
- Understand key definitions related to the menopause transition
- Identify useful references to guide clinician knowledge and treatment
- Share patient education resource

# Take homes

- You are not alone if you feel unprepared to address menopause
- NO lab test can determine if someone is perimenopausal
- Common symptoms are treatable!
- NAMS summaries (now the Menopause Society) for clinician education
- Mymenoplan.org for patient education



# 1. History of Menopause Research

Estrogen-only HT first came into practice

1960s

Associations shown between HT use and lower rates of CHD, osteoporosis, dementia, and overall mortality in analyses from Nurses Health Study and other observational studies

This resulted in increased prescriptions, making estrogens some of most prescribed medications

1980s, 1990s

WHI estrogen-alone trial stopped early after average follow-up 6.8 years owing to risks outweighing or equaling preventive benefits

2004

Many studies have clarified that the benefit:risk ratio of HT is more favorable in women starting treatment at age <60 or <10 years after menopause onset than in those starting in later menopause. Also, on the basis of mostly observational studies, lower risks of some outcomes have been found for transdermal than for oral estrogens and for micronized progesterone than for medroxyprogesterone acetate

2002-present

### 1975

Estrogen found to increase risk of endometrial cancer

Adding progestogens for women with uteruses found to protect endometrium and eliminate risk

### 1993

Women's Health Initiative RCTs and observational studies began

### 2002

WHI estrogen+progestin trial stopped early after average follow-up 5.2 years owing to risks outweighing preventive benefits

WHI publication followed by 33% decline in estrogen therapy and 66% decline in combined HT in US in first year

HT prescriptions decreased 25-40% in UK and Germany

### Today

Few women who would benefit receive HT

Duralde E R, Sobel T H, Manson J E. 2023. Management of perimenopausal and menopausal symptoms.
 BMJ 2023; 382 :e072612 doi:10.1136/bmj-2022-072612

# 2. Timeline of events/Definitions

### Peri-menopause

- Most symptomatic phase
- Menstrual, vasomotor, genitourinary
- Avg 7 years (1-10)

### Menopause

- 12 months no period
- Average age 51
- FSH > 25

# Last menstrual period

- Hard to know when it will "the last one"
- Don't forget those chemical or surgically induced

### Post-menopause

Can be over ½ someone's life

# 3. What is going on ?!?

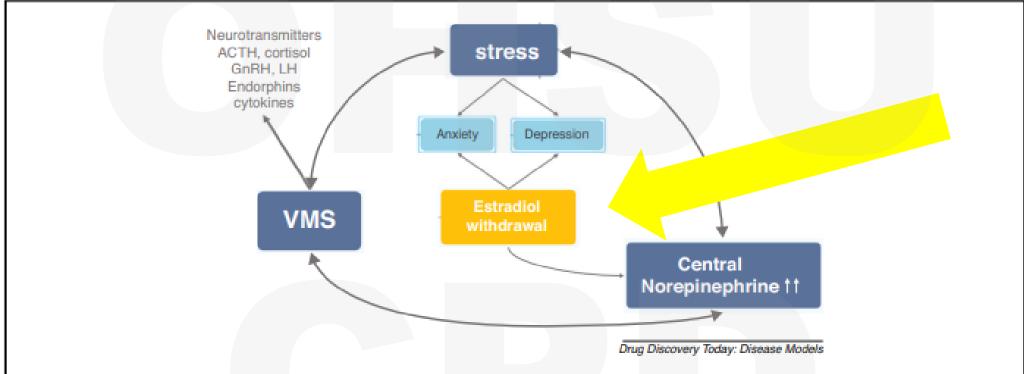
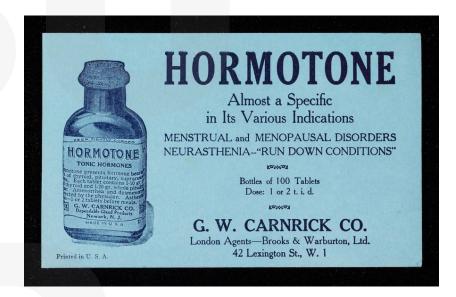


Fig. 4. The two major factors fundamentally responsible for causing hot flushes and night sweats (vasomotor symptoms, VMS) are estradial withdrawal from an estrogen-exposed brain and emotional stress. The estradial withdrawal reason for hot flushes decreases over time while the stress etiology increases because of a "vicious circle" in which initial VMS releases stress-related neurotransmitters causing anxiety, depression and sleep disturbances that perpetuate VMS. In addition, estradial withdrawal is causal in some anxiety and depression which then increase central norepinephrine and thus the risk for VMS.

Source: Fan, Tan, Prior & Chen. 2020. Paradigm shift in pathophysiology of vasomotor symptoms: Effects of estradiol withdrawal and progesterone therapy. Drug discovery today: disease models. Vol 32. pg. 59-69

# 4. Menstrual Irregularities-

- What to expect
  - Skipping periods or prolonged cycle length is normal
- Can approach with hormonal contraception (Not HRT levels)
  - *PERI*menopausal people can conceive if exposed to sperm
- However heavy/gushy, prolonged, painful, random, or frequent
  - NOT normal
- Evaluation- endometrial biopsy
  - Transvaginal ultrasound "normal stripe" misses atypia in Black people
    - Higher prevalence of fibroids in this population



# 5 &6. Vasomotor symptoms

- Hot flashes, sweats
- Sleep, quality of life, work, financial implications
- Hormonal and nonhormonal treatment options
- Individual approach



# Vasomotor symptoms (VMS)

### NAMS Position Statement

The 2023 nonhormone therapy position statement of The North American Menopause Society

### NAMS Position Statement

The 2022 hormone therapy position statement of The North American Menopause Society

## 5. VMS- nonhormonal

- Gabapentin- up to 900mg/day
- SNRIs/SSRIs
  - Paroxetine with FDA indication
    - Shortest half-life of SSRIs so withdrawal symptoms common
  - Escitalopram, citalopram
    - Sertraline, fluoxetine less evidence
  - SNRIs improvement ~ 2 weeks
- Many common supplements are no better than placebo
  - Cost vs. benefit per patient

TABLE 2. Treatment recommendations for nonhormone therapies for vasomotor symptoms with levels of evidence

Category	Treatment	Recommended	Not recommended
Lifestyle			
	Cooling techniques		Level II
	Avoiding triggers		Level II
	Exercise		Level II
	Yoga		Level II
	Dietary modifications		Level III
	Weight loss	Levels II-III	
Mind-body	techniques		
	Cognitive-behavioral	Level I	
	therapy		
	Mindfulness-based		Level II
	interventions		
	Clinical hypnosis	Level I	
	Paced respiration		Level I
	Relaxation		Level II
Prescription	therapies		
	SSRIs/SNRIs	Level I	
	Gabapentin	Level I	
	Pregabalin		Level III
	Clonidine		Levels I-III
	Oxybutynin	Levels I-II	
	Suvorexant		Level II
	Fezolinetant	Level I	
Dietary sup	plements		
	Soy foods		Level II
	and soy extracts		
	Soy metabolites equol		Level II
	Supplements/Herbal		Levels I-III
	remedies <sup>a</sup>		
	Cannabinoids		Level II
Acupunctur	re, other treatments, and te	hnologies	
	Acupuncture		Level II
	Stellate ganglion block	Levels II-III	
	Calibration of neural	20101011111	Level II
	oscillations		
	Chiropractic intervention		Level II

Level I, good and consistent scientific evidence; Level II, limited or inconsistent scientific evidence; Level III, consensus and expert opinion.

SNRIs, serotonin-norepinephrine reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors.

Pollen extract, ammonium succinate, Lactobacillus acidophilus, rhubarb, black cohosh, wild yam, dong quai, evening primrose oil, maca, ginseng, labisia pumila/eurycoma longifolia, chasteberry, milk thistle, omega-3 fatty acids, vitamin E.

# 6. VMS-hormonal

Source: Crandall CJ, Mehta JM, Manson JE. Management of Menopausal Symptoms: A Review. *JAMA*. 2023;329(5):405–420.

doi:10.1001/jama.2022.24140

Figure 1. Suggested Clinical Approach to Prescribing Menopausal Hormone Therapy

### Assessment of menopausal vasomotor symptoms (VMS)

· Hot flashes, night sweats, or both

### Moderate to severe VMS:

Bothersome, interfering with quality of life, or both, including sleep quality or daytime function

### Mild VMS:

Not interfering with quality of life

Do not consider hormone therapy (HT)

### Assessment of contraindications to HT use

- · History of breast cancer
- Liver disease
- History of stroke or myocardial infarction
- Known or suspected estrogen-dependent neoplasia
- · History of deep vein thrombosis or pulmonary embolism
- Thrombophilic disorders (eg, protein C, protein S, or antithrombin deficiency)

### Contraindications not present

### Contraindications present or no interest in HT

### Selection of HT preparation (based on patient preference)

Best candidates for starting HT are younger than age 60 y, are within 10 y since menopausal onset, and do not have elevated risks for cardiovascular disease or breast cancer

Estrogen only (for people with previous hysterectomy)
Estrogen plus progestogen or bazedoxifine (for people with uterus in situ)

### Considerations for transdermal HT use

- May have less adverse effects on clotting factors (and possibly venous thromboembolism) than oral HT
- May be safer for women with risk factors for cardiovascular disease (effects on cardiovascular events and breast cancer outcomes have not been determined in RCTs)

### Consider rates of endometrial hyperplasia with HT usea

Promptly evaluate vaginal bleeding during HT use

### Consideration of nonhormonal alternatives

Options that are off-label (except paroxetine), but supported by clinical trial data

- 37.5 mg/d of extended-release venlafaxine for 1 wk, then increase to 75 mg/d
- 100 mg/d of desvenlafaxine
- 10 mg/d of escitalopram (may increase to 20 mg/d)
- 7.5 mg of paroxetine mesylate every night at bedtime
- 10 mg/d of citalopram (may increase to 30 mg/d)
- 900 mg/d of gabapentin at night or in divided doses
- 75 mg of oral pregabalin twice/d (may increase to 150 mg twice/d)
- 0.1-1 mg/d of oral clonidine or 0.1-0.3 mg/wk of transdermal clonidine

# Which form?

Preparation	Generic Name	Daily Dosage
Combination hormone therapy (for women with a uterus)		
Oral continuous	CEs and MPA	0.625 mg CE plus 2.5 or 5.0 mg MPA; 0.45 mg CE plus 2.5 mg MPA; or 0.3 or 0.45 mg CE plus 1.5 mg MPA
Oral continuous	Estradiol and norgestimate	1 mg estradiol (days 1-3) 1 mg estradiol and 0.09 mg norgestimate (days 4-6)
Oral sequential	CEs and MPA	0.625 mg CE plus 5.0 mg MPA
Transdermal continuous	17β-estradiol-norethindrone acetate	1.0 mg estradiol plus 0.5 mg norethindrone 0.05 mg estradiol plus 0.14 or 0.25 mg norethindrone (patch applied twice weekly)
Transdermal continuous	17β-estradiol-levonorgestrel	0.045 mg estradiol plus 0.015 mg levonor- gestrel (patch applied weekly)
Unopposed estrogens (for women without a uterus)		
Oral	CEs	0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg
Oral	17β-estradiol	0.5 mg, 1.0 mg, 2.0 mg
Transdermal	17β-estradiol	0.025 mg, 0.05 mg, 0.075 mg, 0.1 mg (patch applied twice weekly)
Transdermal	Estradiol patch	0.025 mg, 0.0375 mg, 0.05 mg, 0.075 mg, 0.1 mg (patch applied weekly)

CE = conjugated estrogen; MPA = medroxyprogesterone.

Source: Melissa A. McNeil, Sarah B. Merriam. Menopause. Ann Intern Med.2021;174:ITC97-ITC112. [Epub 13 July 2021]. doi:10.7326/AITC202107200

# WHI Findings of Total Cohort Ages 50-79 at enrollment

Event	E+P		E alone	
	Relative Risk	Absolute Risk (per 10,000 women)	Relative Risk	Absolute Risk (per 10,000 women)
CHD	1.29*	7 more	0.91	5 fewer
Stroke	1.41*	8 more	1.39*	12 more
VTE	2.11*	18 more	1.33	7 more
Breast CA	1.26	8 more	0.77	7 fewer
Colorectal CA	0.63*	6 fewer	1.08	1 more
Hip Fracture	0.66*	5 fewer	0.61*	6 fewer
Death	0.98	1 less	1.04	3 more
Global Index	1.15*	19 more	1.01	2 more

<sup>\*</sup>Statistically significant in primary analysis, *p*<0.05 *JAMA* 2002, 288:3, p321-333, Risk/benefits E+P in healthy postmenopausal women. *JAMA* 2004, 291:14, p 1701-12, Effects of CEE in health postmenopausal women.

# 7. Mood

### Consensus Recommendations

Guidelines for the evaluation and treatment of perimenopausal depression: summary and recommendations

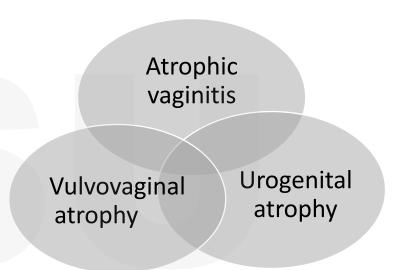
- Vulnerable window in menopause transition
- Perimenopausal mood changes- irregularly irregular
- Hormone replacement therapy can help in peri-menopause but not post-menopause
- SSRIs, SNRIs, Cognitive behavioral therapy also belief...



# 8. Sex (and urination)

### NAMS Position STATEMENT

The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society



- Lubrication, Lubrication, Lubrication
- Topical estrogen
  - Do no use if undiagnosed vaginal or uterine bleeding
  - Guidance on use in patients with history of breast cancer not consistent
    - ACOG supports use
- Physical exam!
- If not improving with treatment, consider vulvar biopsy for other causes

# 9. So many other symptoms...

- Mymenoplan.org
- NIH funded
- Evidence-based approaches



ABOUT MENOPAUSE SYMPTOMS TREATMENTS TOOLBOX

REATMENTS TOOLBOX WOMEN'S STORIES OUR STORY

### MENOPAUSE SYMPTOMS

Every woman has a unique menopause story. Click on a symptom to learn more about it. Or, match symptoms with potential coping strategies and treatments with the My MenoPlan tool.

### MOST COMMON



Hot Flashes & Night Sweats



Sleep Problems /



Mood, Depression, Anxiety

### VAGINA AND SEX



Heavy, Irregular Periods



Low Sex Drive



Pain during sex



Vagina Pain, Dryness (not during sex)

10. Layer Approaches

Cognitive **VMS Behavioral** causing Therapy for Insomnia Insomnia Anxiety Disorder

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# Thank you!

