Menopause/Perimenopause for Primary Care

Thursday, September 24, 2026
Kaiser Permanente Administrative Campus
Rainier Bldg Room F111/115

Register Today!

Target Audience

Primary care physicians, advanced practice nurses, physician assistants, and members of the health care team who seek to advance their knowledge in this area.

About the Course

This activity will equip primary care clinicians with an evidence-based, practical approach to menopause and perimenopause management. Through expert-led presentations and case-based discussion, participants will review current evidence, treatment options, and counseling strategies to support individualized, equitable, patient-centered care.

Agenda and Objectives

a.m.

8:00 - 8:10 Welcome and Introductions – Ory Holtzman, MD and Annie Gayman, MD

8:10 - 8 :45 From Panic to Perspective: Understanding the WHI's Lasting Impact on Menopause Care – Shannon Eagle, ARNP, CNM

- *Review the background, original WHI study design, population, and primary outcomes, including limitations that shaped early interpretations.*
- *Discuss how initial media coverage and scientific misinterpretation influenced decades of clinical practice.*
- *Highlight recent evidence that clarifies risks by age, timing of initiation, and type of therapy.*
- *Explore how WHI findings continue to influence patient perceptions, clinician hesitancy, and current guidelines.*

8:45 - 9:15 Menopause and Perimenopause Basics: Recognizing the Spectrum of Symptoms – Annelise Gaaserud, MD and Jessica Huard, MD

- *Review the physiology of ovarian aging and hormonal variability in perimenopause.*
- *Identify vasomotor, cognitive, mood, sleep, and somatic symptoms — including less recognized presentations such as joint pain, palpitations, and genitourinary changes.*
- *Discuss diagnostic challenges: irregular cycles, normal labs, and when testing is (and isn't) useful.*
- *Explore disparities in symptom recognition across racial, cultural, and socioeconomic groups.*

9:15 - 10:00 MHT Options, Risks, and Benefits: Building an Individualized Treatment Plan – Mary Welch, MD

- *Review absolute and relative contraindications to systemic HRT.*
- *Discuss risk stratification for breast cancer, VTE, stroke, and cardiovascular disease.*
- *Explore shared decision-making frameworks that incorporate patient values, symptom burden, and risk tolerance.*
- *Outline practical algorithms for choosing expectant management, non-hormonal therapies, or specific HRT formulations.*

10:00 - 10:15 Break

10:15 - 10:45 Prescribing HRT with Confidence: Pharmacology, Formulary Tools, and Practical Pearl
– Galen Goertzen, PharmD, BCACP

- *Compare pharmacology of oral vs transdermal estrogen, and micronized vs synthetic progestins.*
- *Demonstrate SmartRx and formulary tools to identify covered options, cost-effective choices, and prior authorization pitfalls.*
- *Evaluate common supplements marketed for menopause: evidence, safety, and counseling strategies.*
- *Introduce compounding basics: when it's appropriate, regulatory considerations, and how to counsel patients about risks.*

10:45 - 11:15 Case Studies in Perimenopause – Panel of morning presenters. Moderator: Annie Gayman, MD

- *Analyze real-world cases to identify diagnostic and management challenges.*

11:15 - 12:00 Sexual Well-Being in Midlife: Evidence-Based Approaches – Andrew Warner, MD

- *Screen for sexual health concerns in midlife*
- *Discuss the role of estrogen, androgens, pelvic floor function, and psychosocial factors in sexual health.*
- *Explore evidence for testosterone therapy: indications, dosing principles, safety considerations, and monitoring.*
- *Compare FDA-approved vs compounded testosterone options and how to counsel patients about off-label use.*

12:00 - 1:00 Lunch

1:00 - 1:30 Genitourinary Syndrome of Menopause – Jessica Yearwood, MD, MSCP

- *Review diagnostic criteria and common presentations, including urinary urgency, dyspareunia, and recurrent UTIs.*
- *Compare local estrogen therapies, DHEA, ospemifene, and non-hormonal options.*
- *Discuss long-term maintenance strategies and patient counseling.*
- *Address safety concerns in patients with a history of breast cancer.*

1:30 - 2:00 Menopause and Cardiovascular Health – Rachael Wyman, MD

- *Evaluate the impact of menopause on cardiovascular risk*
- *Review how estrogen decline affects lipid profiles, vascular function, and metabolic health.*
- *Discuss timing of HRT initiation and cardiovascular risk modification.*

2:00 - 2:30 Pelvic floor Health in Menopause – Melinda Wescott, PT and Natasha Hennings, PT

- *Review how hormonal changes affect pelvic floor musculature, connective tissue, and continence.*
- *Discuss evidence-based exercise programs, physical therapy referrals, and behavioral strategies.*

2:45 - 3:15 Fueling the Midlife Body: Nutrition for Symptom Relief and Long-Term Health
– Nicole Merriam, MS, RD, CDCES

- *Review metabolic shifts in perimenopause and menopause, including changes in insulin sensitivity and body composition.*
- *Discuss evidence-based dietary recommendations.*
- *Address weight stigma, realistic goal-setting, and culturally sensitive nutrition counseling.*

3:15 - 4:00 Influencers, Algorithms, and "Menopause Clinics": What Patients Are Hearing

– Ory Holtzman, MD

- *Explore the commercialization of menopause and why it has become a booming industry.*
- *Analyze common claims made by influencers, telehealth prescribers, and wellness brands.*
- *Discuss how to counsel patients who arrive with extensive lab panels, supplement regimens, or requests for compounded hormones or pellets.*
- *Provide strategies for redirecting patients toward evidence-based care without dismissing their concerns.*
- *Review regulatory issues and safety considerations around compounding.*

4:00 - 4:30 Faculty Q&A and wrap up – All faculty

- *Synthesize key takeaways from the day's sessions*

Faculty and Planners

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Washington Permanente Medical Group

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Medical Program Director of Midwifery
Olympia Medical Center
Washington Permanente Medical Group

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Accreditation

Kaiser Foundation Health Plan of Washington is accredited by the Washington State Medical Association CME Accreditation Committee to sponsor continuing medical education for physicians.

Kaiser Foundation Health Plan of Washington designates this educational activity for a maximum of **7.00 hours** in Category 1 to satisfy the relicensure of the Washington State Medical Quality Assurance Commission.

Kaiser Foundation Health Plan of Washington designates this live activity for a maximum of ***7.00 AMA PRA Category 1 Credit(s)™.*** Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Tuition and Registration

Kaiser Permanente Staff	$175
Community Attendees	$195

Click Here to Register!

Your early registration is important! It helps us confirm attendance and determine if the course will proceed as scheduled. Thank you for registering promptly!

Location

Kaiser Permanente Administrative Campus - Rainier Bldg
Room F111/115
2715 Naches Ave. SW
Renton, WA 98057

For More Information:

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Clinical Knowledge, Education, and Technology
KP Medical Foundation



From Panic to Perspective: Understanding the WHI's Lasting Impact on Menopause Care

Shannon Eagle, CNM, ARNP, DNP
Service Line Medical Director, Midwifery
09/24/2026

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Outline

- Background/ history of Menopause Hormone Therapy (MHT)
- The Women's Health Initiative (WHI)
- Literature Update Beyond the WHI
- WHI re-analysis

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Early Understanding of Menopause

Early Greek and Roman Physicians thought monthly menstruation was purging toxins and poisons from the body and when menstruation ended in menopause a failure to release toxins that would eventually drive a women into “menopausal madness”



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Landmark Article
Sept 8, 1923
(*JAMA* 1923;81:819-821)

An Ovarian Hormone

Preliminary Report on Its Localization, Extraction and Partial Purification, and Action in Test Animals*

Edgar Allen, Ph.D. and Edward A. Doisy, Ph.D.

St. Louis

The fact that double ovariectomy abolishes the cyclic changes which normally occur in the genital tract of female mammals demonstrates that these changes are due to some influence from the ovaries. That this influence is hormonal in nature is indicated by the maintenance of cyclic changes by autotransplantation of the ovaries to other sites in the body.[1] Many attempts have been made to localize the seat of production of an internal secretion in definite ovarian structures. The follicles, the corpora lutea[2] developing in them after ovulation, and the interstitial tissue[3] have all been cited as possible sources, and many different ovarian preparations have been used clinically in the belief that therapeutic effects were being secured from accompanying hormones.

But there appears to be no conclusive evidence of either a definite localization of the hypothetic hormone or of the specific effect claimed for the commercial ovarian extracts in wide clinical use. The recent reviews of Frank[4] and of Novak[5] may be cited to illustrate the well founded skepticism concerning the activity of commercial preparations. The reason for this distrust is the absence of any suitable test for the activity of ovarian extracts. Without a practicable test, the search for any hormone is obviously a very haphazard and uncertain task. With a suitable test it has been relatively easy to establish the seat of production of the ovarian hormone of estrus, to observe its effect on animals, and to study methods for its extraction and preliminary purification.

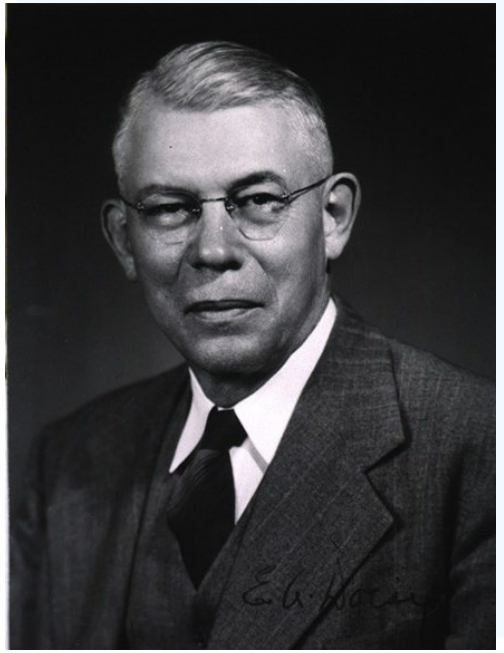
THE TEST METHOD

In 1917, Stockard and Papanicolaou[6] described an exact method for following estrual changes in the living guinea-pig. This method has been applied to the correlation of estrual phenomena in the genital organs of the rat[7] and the mouse.[8] During the anabolic phase of the cycle in these rodents, the epithelium of the vagina grows to a considerable thickness and a cornified layer similar to that in the epidermis develops. During the catabolic phase, the outer layers of this epithelium degenerate and are removed by leukocytic action. These changes provide a definite succession of cell types in the vaginal lumen, each one characteristic of a certain phase of the cycle. Thus the microscopic examination of vaginal smears is a reliable indicator of the estrual condition of the living animal.

*From the Departments of Anatomy, Biologic Chemistry and Surgery, Washington University Medical School, St. Louis, with the assistance of Byron F. Francis, Harry V. Gibson, Leroy L. Robertson, Cleon E. Colgate and William B. Kountz.

1. Marshall, F. H. A.: The Physiology of Reproduction, 1922, p. 220.

6. Stockard, C. R., and Papanicolaou, G. N.: Existence of a Typical Oestrous Cycle in the Guinea-Pig, with a Study of Its Histological and



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Initial FDA Approved Hormones

Emmenin: was an early oral estrogen medication made from human placental extracts and the urine of pregnant women during the 1920s and 1930.

Premarin: **Pregnant Mare Urine**

Diethylstilbestrol (DES): a synthetic estrogen, was the first synthetic hormone approved by the FDA in 1941. Formulated to treat menopausal symptoms, vaginitis, and later widely prescribed to prevent miscarriages. A small number of exposed women develop clear cell adenocarcinoma, a rare cancer of the vagina or cervix.

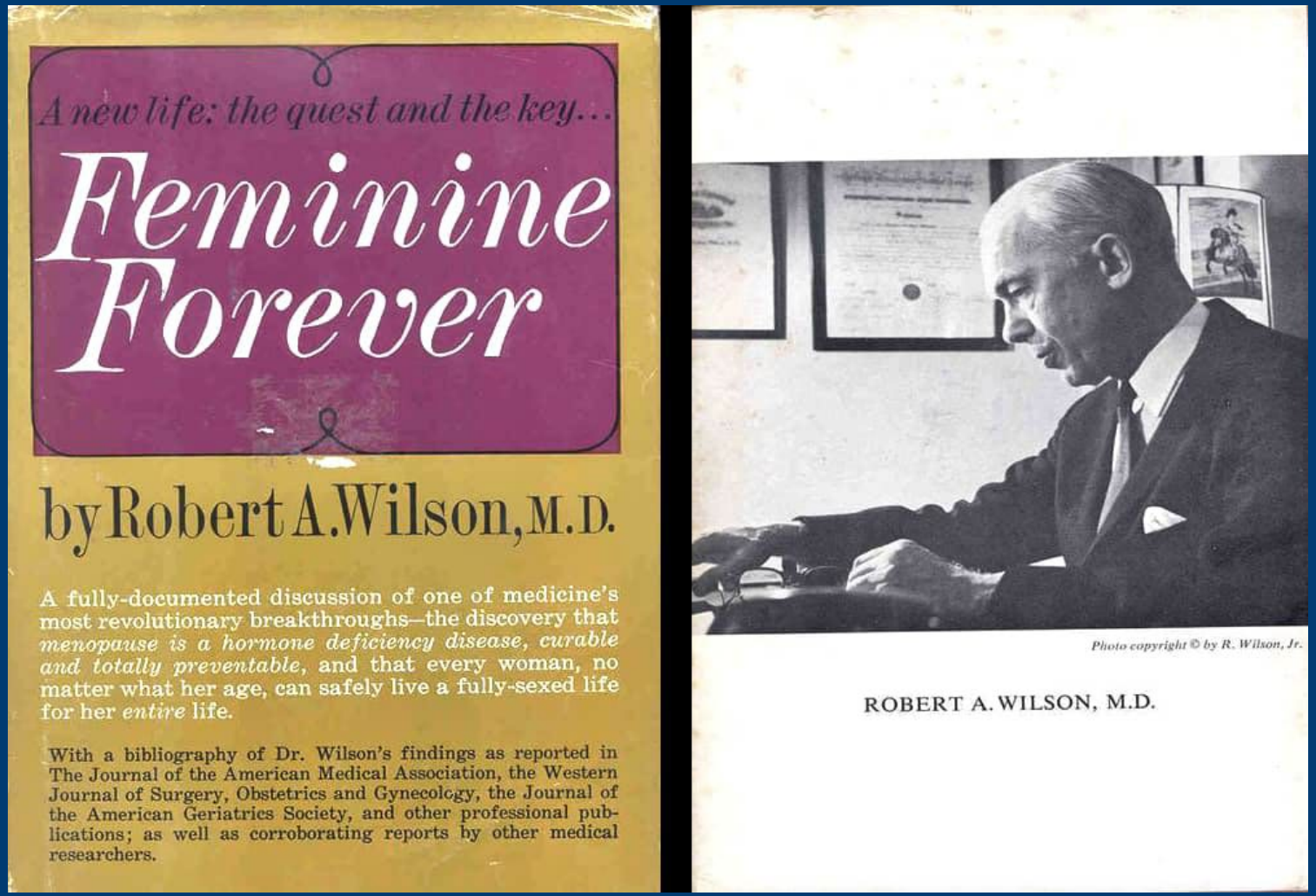


Conjugated Equine Estrogens (Premarin): Approved by the FDA in 1942, this blend of estrogen extracted from pregnant mare urine became the standard treatment for menopausal hot flashes and related symptoms.

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1966: Feminine Forever



"All post-menopausal women are castrates," Wilson wrote. But, with HRT, a woman's "breasts and genital organs will not shrivel. She will be much more pleasant to live with and will not become dull and unattractive."

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Evolving Understanding of Risks and Benefits

- 1975: Association between unopposed estrogen use and endometrial hyperplasia and carcinoma
- 1980s: Endometrial protection through the addition of a progestin
- Reports of preservation of bone mineral density, prevention of osteoporosis
- Controversy over cardiovascular risk and benefit
  - Framingham Heart Study showed CV harm
  - Nurse's Health Study, Leisure World Study, and KP study all showed CV risk reduction

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Women's Health Initiative (WHI) Study

- Randomized control trial (RCT) designed to determine whether postmenopausal HT should be offered to all women to reduce the incidence of CVD
  - Clinical Trials: 68,132 women participated in one or more randomized controlled trials evaluating hormone therapy, dietary modifications, or calcium and vitamin D supplements.
  - Observational Study: 93,676 women enrolled in the long-term observational cohort.
- Given the relatively low incidence of cardiovascular events in younger women, an older cohort was purposefully recruited to adequately power the study. Mean age was 63, largely >10 years post-menopause.
- Budget of more than $600 million

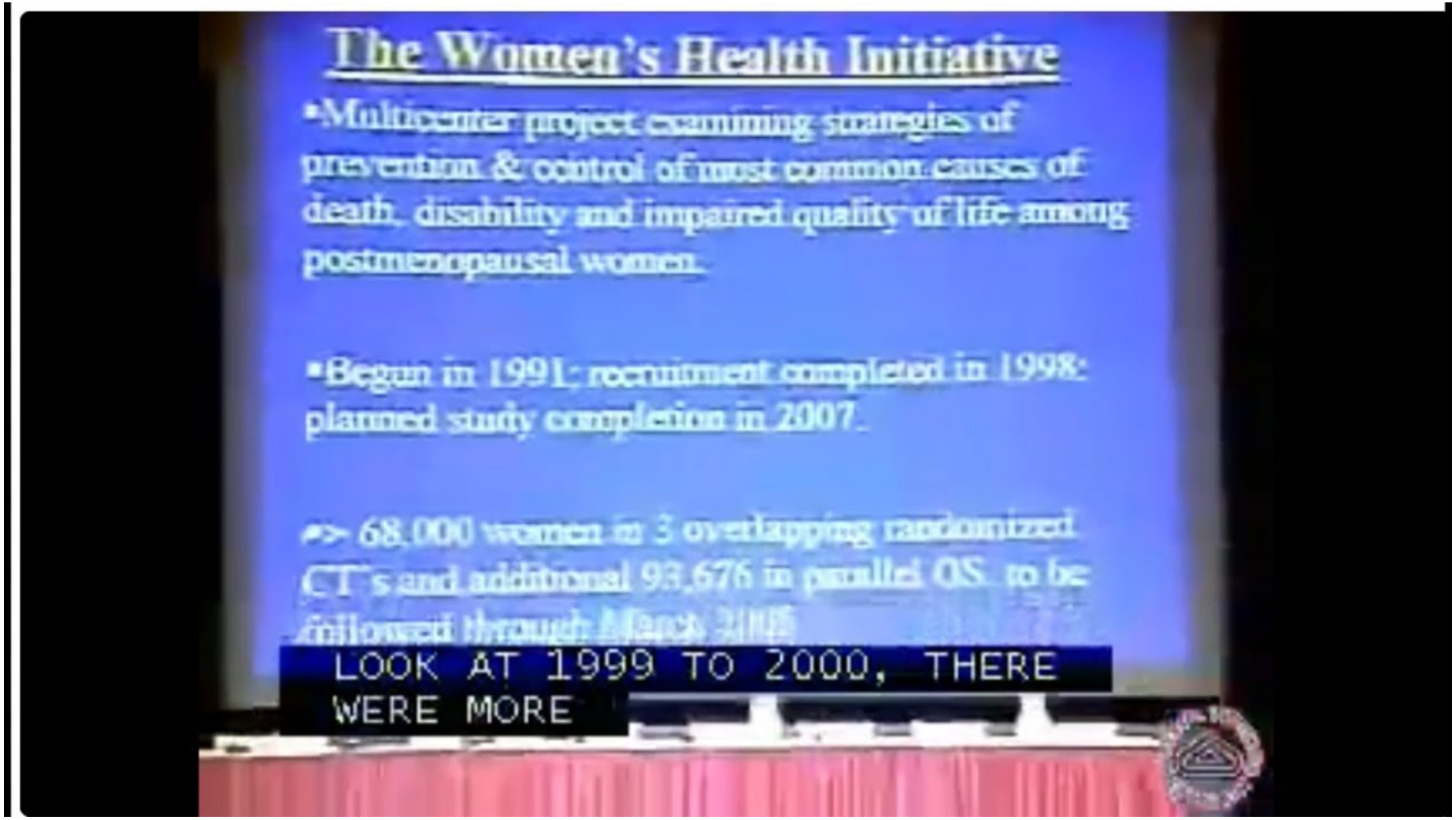


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The Press Conference Heard around the World

- July 9th, 2002 NIH press conference: the preliminary findings focused on the harms of HRT



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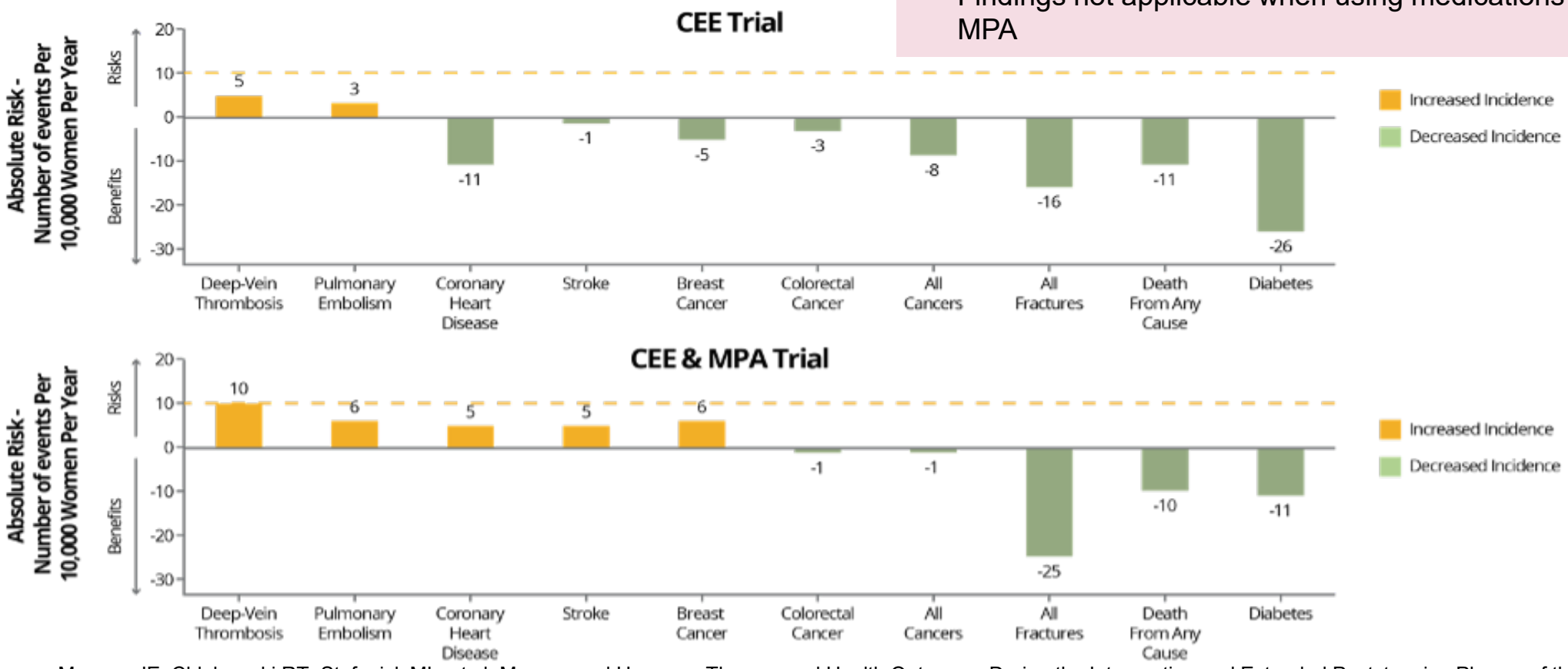
WHI Results

Key takeaways:

- Risk of CHD, breast cancer, stroke, PE, and DVT all increase with CEE and MPA
- Decrease risk of colorectal cancer, fractures, and all-cause mortality

Weaknesses of this study:

- Not powered for age-related subset analyses, so data not statistically significant
- Study population almost a decade older than typical menopause age
- Unusually low breast cancer incidence in the placebo group, specifically participants who were previously on menopausal HT (25% of the study population)
- Findings not applicable when using medications other than CEE and MPA



Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal Hormone Therapy and Health Outcomes During the Intervention and Extended Poststopping Phases of the Women's Health Initiative Randomized Trials. JAMA. 2013;310(13):1353–1368. doi:10.1001/jama.2013.278040

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Conjugated equine estrogen versus estradiol-17B

- Some estrogen that occur in horses do not occur in humans
- There are two unique estrogen receptors, α and β, which were cloned in 1996. Estradiol binds equally to α and β, while CEE favors the β receptors.
- CEE is far more active in increasing inflammatory markers C-reactive protein and inducing matrix metalloproteinase 9



Yas¸ar P, Ayaz G, User SD, Güpür G, Muyan M. Molecular mechanism of estrogen-estrogen receptor signaling. Reprod Med Biol 2016;16:4–20. doi: 10.1002/rmb2.12006

Berrodin TJ, Chang KC, Komm BS, Freedman LP, Nagpal S. Differential biochemical and cellular actions of Premarin estrogens:distinct pharmacology of bazedoxifene-conjugated estrogens combination. Mol Endocrinol 2009;23:74–85. doi: 10.1210/me.2008-0366

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Medroxyprogesterone Acetate vs Micronized Progesterone

Medroxyprogesterone acetate (MPA)

- MPA binds the progesterone receptor but also acts as a glucocorticoid agonist and has androgenic properties, with a longer half-life.
- Increases insulin-like growth factor 1, resulting in increased insulin resistance

Micronized progesterone (MP)

- Is natural progesterone in a micronized formulation that improves oral bioavailability. It binds primarily the progesterone receptor, is rapidly metabolized and lacks clinically significant androgenic or glucocorticoid activity and has no estrogenic metabolites.
- Has not been associated with an increase in thrombogenic risk or an increase in breast cancer incidence
- Cannot be used with peanut allergy

Attribute	Micronized progesterone	Medroxyprogesterone acetate
Type	Bioidentical natural progesterone	Synthetic 17-OHP progestin
Off-target receptors	Minimal androgenic/glucocorticoid	Glucocorticoid agonist + androgenic
Breast cancer risk	Lower / neutral early	Higher (WHI, observational)
CV/metabolic profile	More favorable	Adverse vascular/metabolic effects
CNS	Sedating (allopregnanolone)	No significant mood effect
Endometrial protection	Effective (regimen-dependent)	Effective (regimen-dependent)
Tolerability	Less bleeding/breast tenderness; drowsiness	More bleeding, breast tenderness

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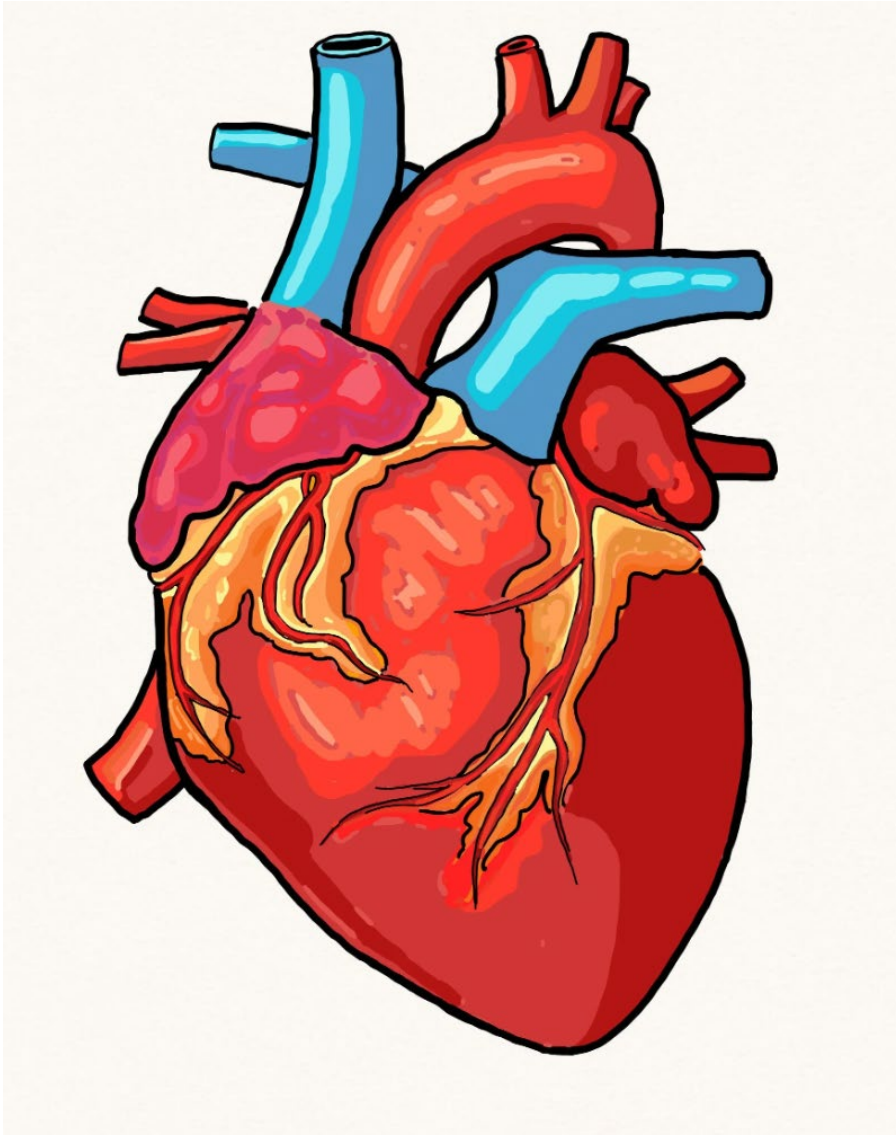
Other Studies of Heart Disease Risk with MHT

ELITE (Early Versus Late Postmenopausal Treatment With Estradiol)

Compared with placebo, 1 mg estradiol-17β (E2) treatment resulted in significantly slower carotid intima–media thickness (CIMT) progression (plaque accumulation), but only among women who initiated estradiol-17β therapy less than 6 years after menopause and only at the 5-year follow-up.

KEEPS (Kronos Early Estrogen Prevention Study)

A 4-year RCT that aimed to evaluate the effects of menopausal HT on atherosclerosis progression as measured by CIMT and coronary artery calcification. After 4 years, neither Premarin nor the Climara (estradiol-17b) patch affected the rate of carotid intima–media thickness progression.



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Other Studies of Risks with MHT

The Nationwide Finnish Comparative Study

Large observational study

A statistically significant breast cancer mortality reduction in women using isomolecular E2 alone (oral E2, transdermal E2 patches, or transdermal E2 gels) compared with a group not using hormones or those using combined menopausal HT (isomolecular estradiol plus a progestin).



DOPS (Danish Osteoporosis Prevention Study)

A randomized 1,006 patients to 2 mg oral E2 plus progestin when indicated or no HT.

Enrolled patients at the onset of menopause and followed them for up to 16 years.

During the 10 years of treatment, compared with placebo, those randomized to menopausal HT experienced significantly lower rates of myocardial infarction, heart failure, or death with no increase in thromboembolism, cancer, or stroke.

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Study of VTE Risk with MHT

TABLE 3 Odds ratios for VTE by specific hormones.

Hormonal exposures	N	Controls (203,590)	Cases (20,359)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
ANY 0–60 d estrogen or progestogen	19,558	17,428	2130	1.25 (1.19-1.31)	1.51 (1.43-1.59)
Estrogen only (MHT)	9650	8735	915	1.07 (0.99-1.15)	1.13 (1.04-1.23)
Oral	6638	5907	731	1.26 (1.17-1.36)	1.33 (1.21-1.46)
Estradiol	3680	3294	386	1.20 (1.08-1.33)	1.24 (1.09-1.40)
CEE[b]	2746	2426	320	1.34 (1.19-1.51)	1.46 (1.28-1.68)
Other estrogens	212	187	75	1.36 (0.90-2.07)	1.39 (0.87-2.24)
Transdermal/estradiol	2885	2713	172	0.65 (0.56-0.76)	0.70 (0.59-0.84)
Vaginal/estradiol ester[c]	106	97	9	0.95 (0.48-1.87)	1.04 (0.44-2.46)
IM/Estrogen[d]	21	18	3	1.68 (0.50-5.70)	0.38 (0.08-1.77)
Estrogen + progestogens (MHT)	5160	4727	433	0.94 (0.85-1.03)	1.22 (1.10-1.38)
Oral	3947	3582	365	1.04 (0.93-1.16)	1.40 (1.24-1.59)
Estradiol + any progestogen	1995	1844	151	0.84 (0.71-0.99)	1.14 (0.95-1.37)
Estradiol + norethindrone	1014	945	69	0.75 (0.58-0.95)	1.03 (0.78-1.35)
Estradiol + other	981	899	82	0.93 (0.74-1.17)	1.25 (0.97-1.61)
CEE/MPA[e]	1519	1363	156	1.17 (0.99-1.38)	1.52 (1.25-1.84)
Ethinyl estradiol + norethindrone	413	358	55	1.57 (1.18-2.09)	2.35 (1.71-3.25)
Other estrogens/other progest	20	17	3	1.81 (0.53-6.18)	1.33 (0.25-7.14)
Transdermal/estradiol + progest[f]	1213	1145	68	0.61 (0.48-0.78)	0.73 (0.55-0.96)
+Progesterone	487	465	22	0.48 (0.32-0.74)	0.55 (0.34-0.89)
+Micronized progesterone	262	249	13	0.54 (0.31-0.94)	0.63 (0.34-1.19)
+ Norethindrone	304	288	16	0.57 (0.35-0.95)	0.65 (0.36-1.14)
+MPA	55	49	6	1.26 (0.54-2.94)	1.76 (0.69-4.50)
+other	105	94	11	1.18 (0.63-2.20)	1.74 (0.87-3.46)
Estrogen+progest (contraception)	2476	1915	561	3.14 (2.84-3.46)	5.22 (4.67-5.84)
Oral/ethinyl estradiol[g]	2399	1862	537	3.08 (2.79-3.41)	5.11 (4.57-5.73)
Transdermal/ethinyl estradiol	13	11	2	1.92 (0.42-8.65)	5.34 (1.06-26.79)
Vaginal/ethinyl estradiol	64	42	22	5.60 (3.34-9.39)	9.26 (5.31-16.15)
Estrogen/CEE+testosterone (±P)[h]	786	745	41	0.56 (0.41-0.77)	0.49 (0.34-0.71)
Progestogen-only	1486	1306	180	1.43 (1.22-1.67)	1.48 (1.24-1.78)
Progesterone	588	550	38	0.71 (0.51-0.98)	0.83 (0.57-1.20)
Micronized progesterone	223	201	22	1.13 (0.73-1.75)	1.20 (0.73-1.97)
Norethindrone[i]	232	198	34	1.83 (1.27-2.64)	1.99 (1.30-3.03)
MPA	443	357	86	2.51 (1.98-3.17)	2.20 (1.67-2.92)
ANY past estrogen or progest (61-365 d)	5494	4995	499	1.02 (0.93-1.12)	0.94 (0.84-1.05)
NO exposure (ref)	198,897	181,167	17,730	1.00	1.00

Oral estrogens increase the risk of VTE. Transdermal and vaginal estrogens do not.

The risk of MHT with estrogen and progesterone depends on the type of progesterone used

EE strongly associated with increased risk of VTE

Norethindrone and MPA increase risk of VTE while progesterone does not

Susan C. Weller, John W. Davis, Laura Porterfield, Lu Chen, Gregg Wilkinson,Hormone exposure and venous thromboembolism in commercially insured women aged 50 to 64 years,Research and Practice in Thrombosis and Haemostasis,Volume 7, Issue 3,2023,100135,ISSN 2475-0379, https://doi.org/10.1016/j.rpth.2023.100135.(https://www.sciencedirect.com/science/article/pii/S2475037923001073)

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Study of VTE Risk with MHT

Key results

- Non-hormonal risk factors dominated. The largest VTE associations were metastatic cancer (OR 13.66), hospitalization/surgery (OR 8.51), trauma (OR 3.52), overall comorbidity burden (OR 3.51), hypercoagulable condition (OR 3.10), and varicose veins (OR 2.87).
- Hormone exposure conferred comparatively modest risk:
  - Any recent hormone exposure: OR 1.51
  - Unopposed (estrogen-only) menopausal HT: OR 1.13
  - Combined menopausal HT: OR 1.23
  - Combined hormonal contraceptives: OR 5.22 — by far the strongest hormonal signal.

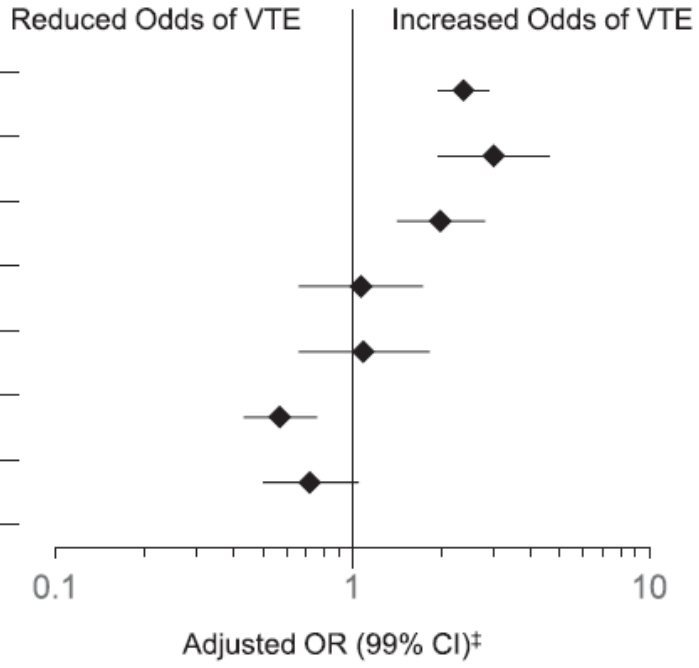


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Association of Progestogens and Venous Thromboembolism Among Women of Reproductive Age



Progestogen*	No. (%) Case Group	Control Group	Crude OR (99% CI)†	Adjusted OR (99% CI)†
DMPA	355 (1.66)	657 (0.61)	2.76 (2.42-3.14)§	2.37 (2.04-2.75)§
NETA	87 (0.41)	114 (0.11)	3.88 (2.93-5.12)§	3.00 (2.17-4.15)§
MPA	111 (0.52)	232 (0.22)	2.43 (1.94-3.05)§	1.98 (1.53-2.58)§
Prog	51 (0.24)	202 (0.19)	1.28 (0.94-1.75)	1.07 (0.75-1.54)
Implant	39 (0.18)	177 (0.17)	1.14 (0.80-1.61)	1.09 (0.74-1.61)
NET	131 (0.61)	724 (0.68)	0.92 (0.76-1.11)	0.57 (0.46-0.71)§
LNG-IUD	77 (0.36)	446 (0.42)	0.88 (0.69-1.13)	0.72 (0.54-0.96)



Cockrum RH, Soo J, Ham SA, Cohen KS, Snow SG. Association of Progestogens and Venous Thromboembolism Among Women of Reproductive Age. Obstet Gynecol. 2022 Sep 1;140(3):477-487. doi: 10.1097/AOG.0000000000004896. Epub 2022 Aug 3. PMID: 35926206; PMCID: PMC9669089.

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Menopausal Hormone Therapy Formulation and Breast Cancer Risk



Type of Hormone	Control Group (n=431,830)	Case Group (n=43,183)	Crude OR (95% CI)	Adjusted OR (95% CI)
Ever any menopausal HT*	62,753 (14.5)	7,280 (16.9)	1.19 (1.16–1.23)	1.12 (1.09–1.15)
Estrogen†				
No estrogen	373,019 (86.4)	36,391 (84.3)	1.0 (Ref)	1.0 (Ref)
Bioidentical	21,579 (5.0)	2,487 (5.8)	1.18 (1.13–1.23)	1.04 (1.00–1.09)
Animal-derived	28,184 (6.5)	3,311 (7.7)	1.20 (1.16–1.25)	1.01 (0.96–1.06)
Both	9,048 (2.1)	994 (2.3)	1.13 (1.05–1.20)	0.96 (0.89–1.03)
Progestogen‡				
No progestogen	410,256 (95.0)	40,352 (93.4)	1.0 (Ref)	1.0 (Ref)
Bioidentical	125 (0.03)	12 (0.03)	0.98 (0.54–1.77)	0.99 (0.55–1.79)
Synthetic	21,434 (5.0)	2,817 (6.5)	1.34 (1.28–1.39)	1.28 (1.22–1.35)
Both	15 (0.0)	2 (0.0)	—	—

OR, odds ratio; HT, hormone therapy; Ref, referent; —, analysis could not be executed owing to insufficient cell numbers.
Data are n (%) unless otherwise specified.
* Adjusted for age, body mass index, smoking status, alcohol consumption, hysterectomy, oophorectomy, history of endometrial cancer, history of family breast cancer, and oral contraceptive use.
† Adjusted for exposure to progestogen therapy and age, body mass index, smoking status, alcohol consumption, hysterectomy, oophorectomy, history of endometrial cancer, history of family breast cancer, and oral contraceptive use.
‡ Adjusted for exposure to estrogen therapy and age, body mass index, smoking status, alcohol consumption, hysterectomy, oophorectomy, history of endometrial cancer, history of family breast cancer, and oral contraceptive use.

Abenhaim HA, Suissa S, Azoulay L, Spence AR, Czuzoj-Shulman N, Tulandi T. Menopausal Hormone Therapy Formulation and Breast Cancer Risk. Obstet Gynecol. 2022 Jun 1;139(6):1103-1110. doi: 10.1097/AOG.0000000000004723. Epub 2022 May 3. PMID: 35675607.

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Re-analysis of the WHI data

- The modern synthesis (post-2007): Age-stratified reanalysis and longer follow-up (up to ~20 years) reframed the WHI findings.
- The critical insight was that WHI participants were, on average, more than a decade past menopause — not the symptomatic 50–59 year-olds who typically seek HRT.
- Absolute risks and the risk: benefit balance differ markedly by age and time since menopause:
    - Initiating before age 60 or within 10 years of menopause carries low absolute attributable risk (generally <1 additional adverse event per 1000 women per year) and may confer favorable or neutral CHD and all-cause mortality effects.
    - Initiating after age 60 or >10 years post-menopause (especially ≥70) increases risks of CHD, stroke, VTE, and dementia.
    - Supporting mechanistic and trial data: the primate atherosclerosis model, ELITE (benefit on carotid IMT only when started within 6 years of menopause), and the Danish Osteoporosis Prevention Study.



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The Menopause Goldrush

Supplements

Compounded hormones

Telemedicine startups

Social media influencers



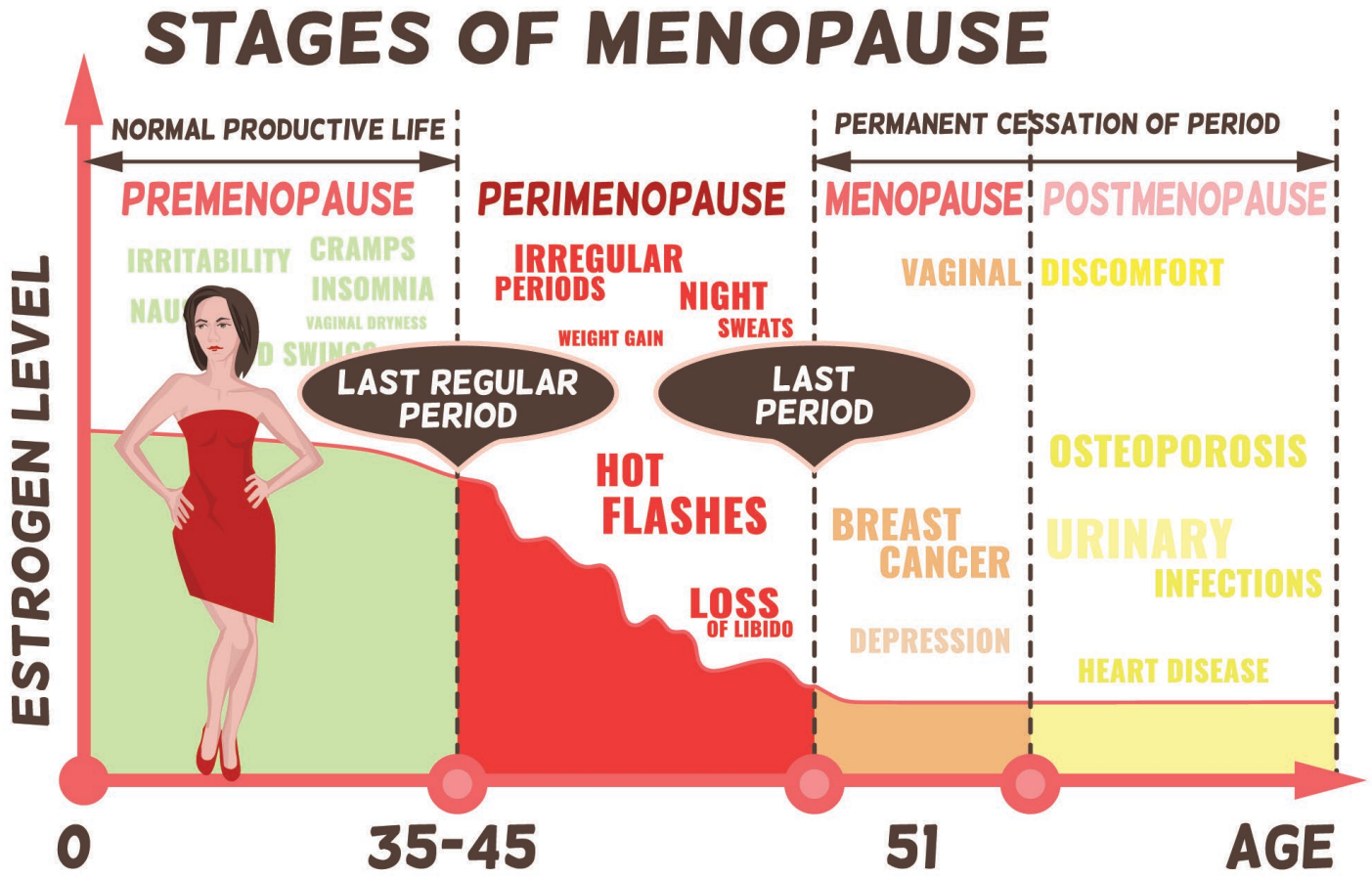


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QUESTIONS?

Whose ready to start prescribing some MHT??



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Menopause and Perimenopause Basics: Recognizing the Spectrum of Symptoms

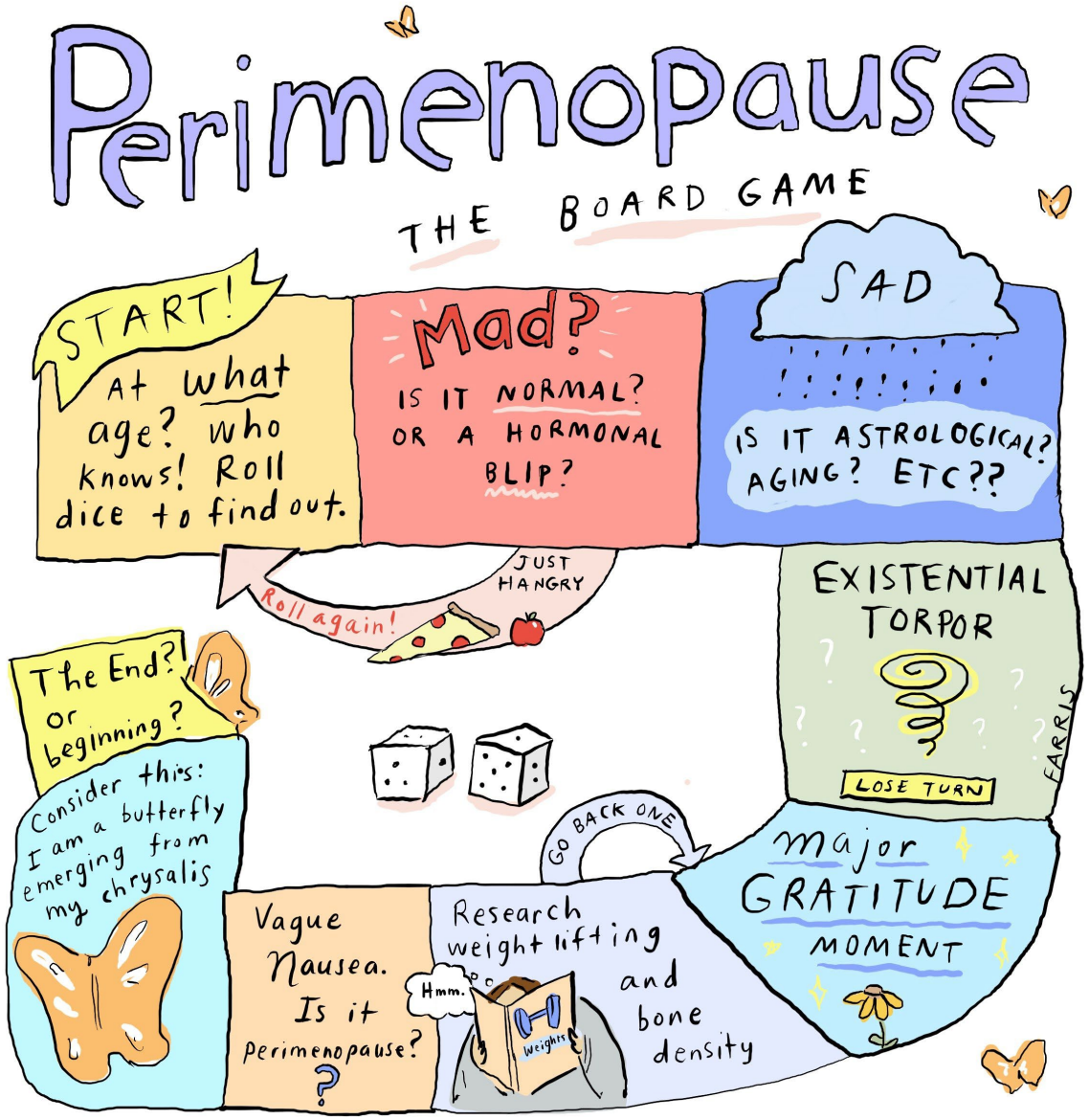
Annelise Gaaserud MD, MPH, Family Medicine with OB.

Jessica Huard MD, OB/GYN

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Introduction

- *Review the physiology of ovarian aging and hormonal variability in perimenopause.*
- *Identify vasomotor, cognitive, mood, sleep, and somatic symptoms — including less recognized presentations such as joint pain, palpitations, and genitourinary changes.*
- *Discuss diagnostic challenges: irregular cycles, normal labs, and when testing is (and isn't) useful.*
- *Explore disparities in symptom recognition across racial, cultural, and socioeconomic groups.*



Definitions

Natural menopause	Permanent cessation of menses for 12 months from loss of ovarian follicular activity.[a]
Induced menopause	Surgical or iatrogenic loss of ovarian function (eg, bilateral oophorectomy, chemotherapy, pelvic radiation, other forms of ovarian toxicity).
Primary ovarian insufficiency	Loss of normal ovarian function before age 40 y, resulting in irregular menstrual cycles and reduced fertility.
Premature menopause	FMP before age 40 y.
Early menopause	FMP before age 45 y.
Late menopause	FMP after the age 55 y.
Perimenopause/Menopause transition/Climacteric	The time frame "around menopause" marked by intermenstrual cycle irregularities or other menopause-related symptoms (hot flashes, sleep problems, vaginal dryness); ends after 1 y of amenorrhea.
Postmenopause	Stage of life after FMP.

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Menopause - Terminology

- Menopause
- A normal, natural event, defined by the final menstrual period (FMP) and confirmed after 1 year of no menstrual bleeding.
- Represents the permanent cessation of menses resulting from loss of ovarian follicular function, usually because of aging.
- Normally occurs between the ages of 40 and 58 years, median age in US is 51 years.

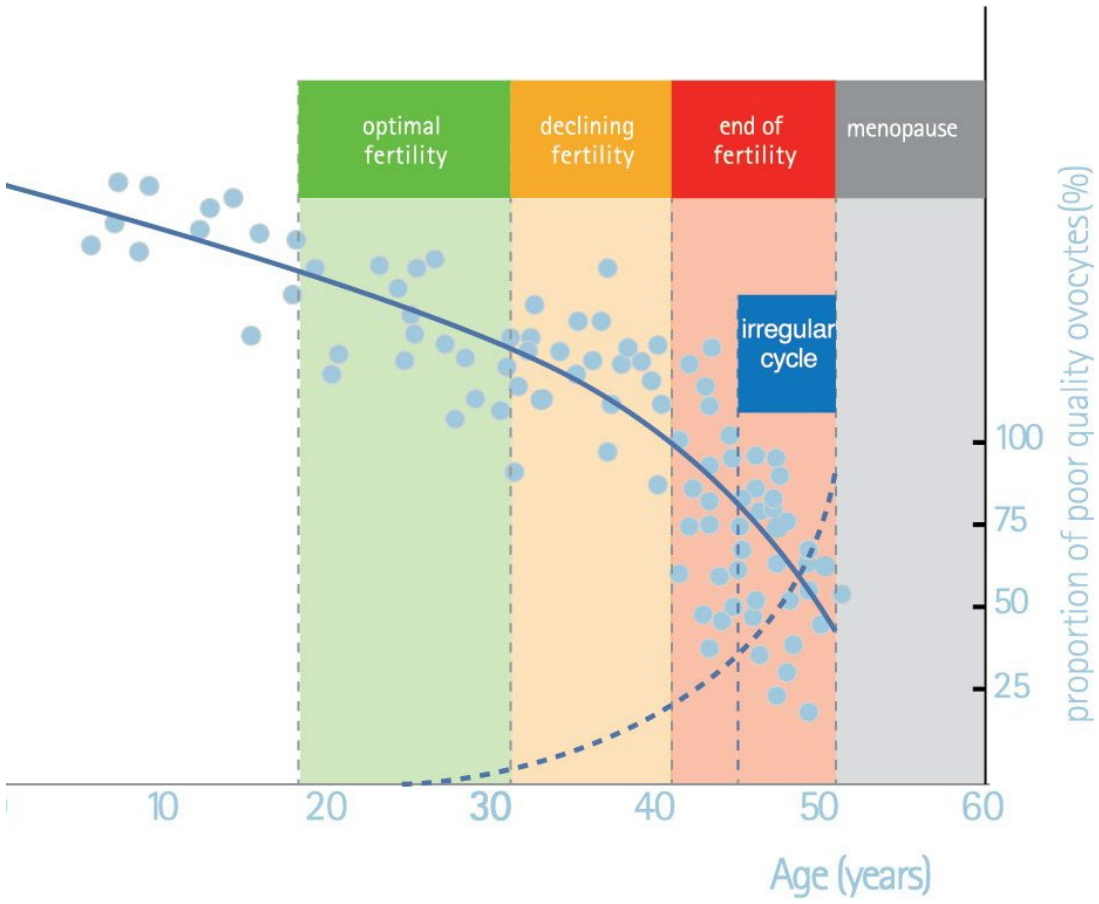
- Primary Ovarian Insufficiency (POI) characterized by hypergonadotropic hypogonadism that can be transient. Affects **1%** of women younger than 40 years old
- Premature Menopause is permanent ovarian failure before age 40
- Early Menopause occurs between ages 40 and 45 in about **3%** of the population
- These early states of menopause are mostly idiopathic though can be due to genetic, autoimmune, iatrogenic, infectious and metabolic causes

Could these symptoms be related to the Menopause Transition?

Each year, about 1.3 million individuals enter menopause (1); up to 80% of people experience vasomotor symptoms (hot flushes, night sweats) during the menopause transition, yet over 1 in 3 with symptoms go unrecognized or undiagnosed. Additionally, an estimated $1.8 billion is lost annually in the U.S. based on workdays missed due to menopause symptoms. (2)

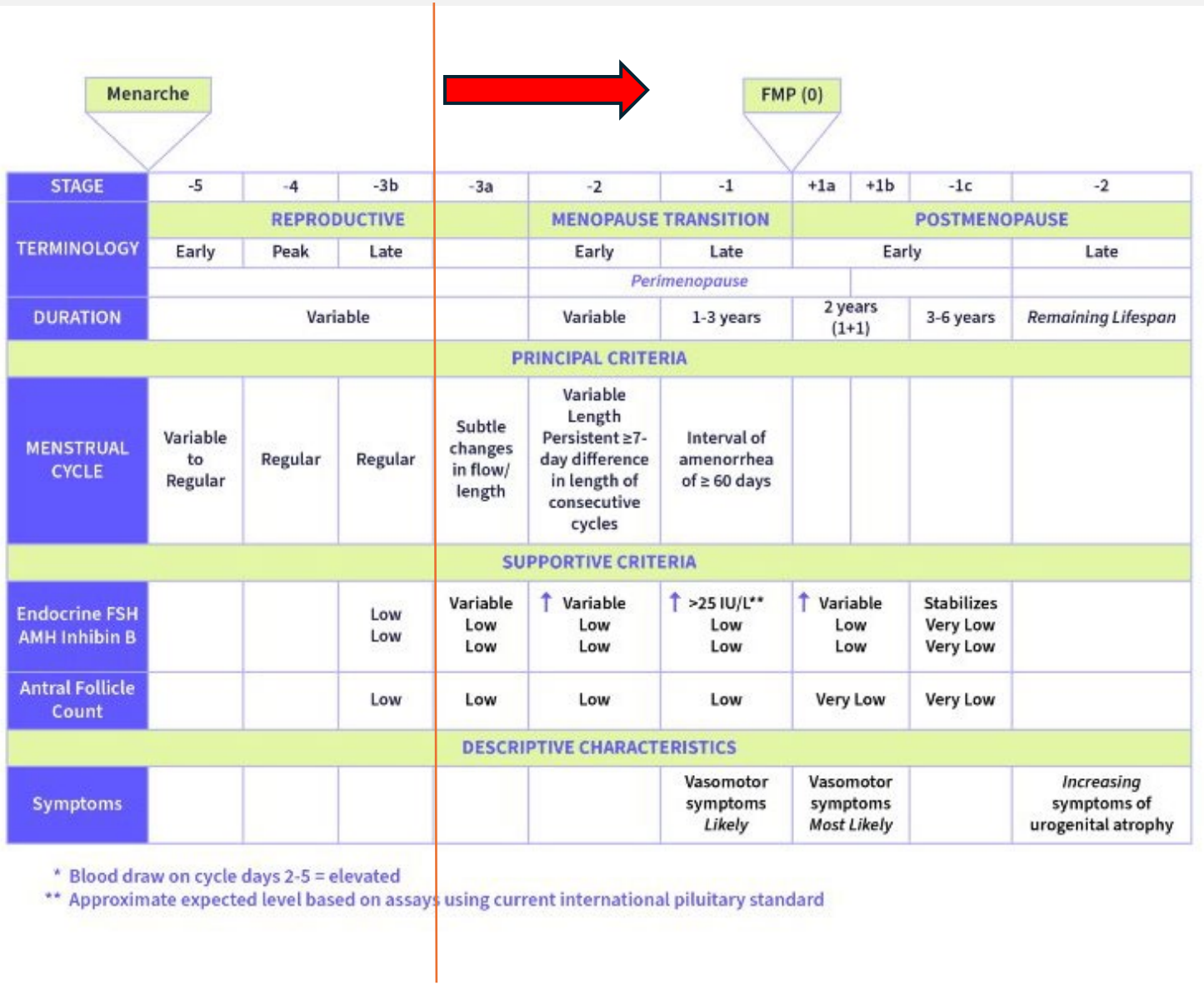
Symptoms during this time can be attributable to either or both chronological aging and reproductive aging (3) or other health conditions.

- Chronological aging: Natural process of physiologic deterioration that is genetically determined and environmentally modifiable
- Reproductive ageing: Progressive loss of oocytes by ovulation and atresia.
    - Not directly correlated with chronologic aging.
    - Ovaries contain a finite number of oocytes.
        - At 20 weeks' gestation: 6 to 7 million oocytes.
        - At birth: 1 to 2 million oocytes.
        - At puberty: 300,000 to 500,000 oocytes.
        - At menopause: 300 to 400 oocytes, most of which are incompetent



Stages of Reproductive Aging

- STRAW+10 updated and modified the model in 2011.
    - Considered the gold standard for categorizing reproductive aging and divides the reproductive lifespan into three broad phases, further broken down into seven stages centered on the FMP (Stage 0).
    - Reproductive Phase: Early (Stage −5), Peak (Stage −4), and Late (Stage –3).
    - **The Menopause Transition (MT): Early (Stage –2) and Late (Stage –1).**
    - **Postmenopause Phase: Early (Stage +1) and Late (Stage +2).**
- Applies to menstruating women regardless of demographics, age, body mass index (BMI), and lifestyle characteristics.



STAGE	-5	-4	-3b	-3a	-2	-1	+1a	+1b	-1c	-2
TERMINOLOGY	REPRODUCTIVE				MENOPAUSE 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 piluitary standard

Hormone levels are predictably unpredictable in perimenopause

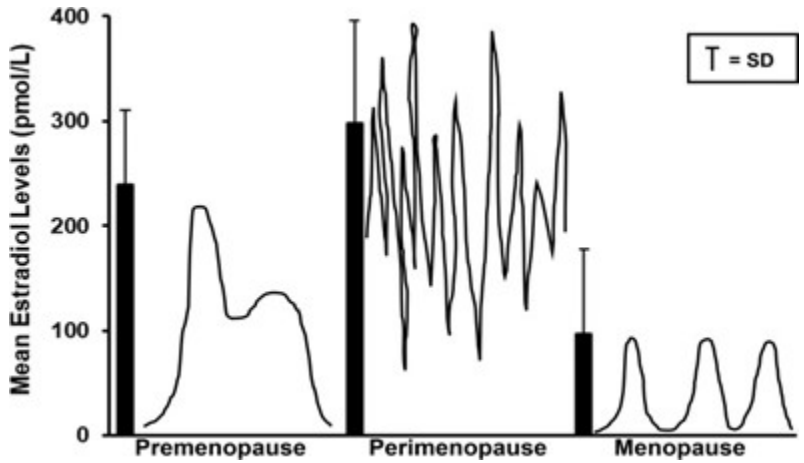
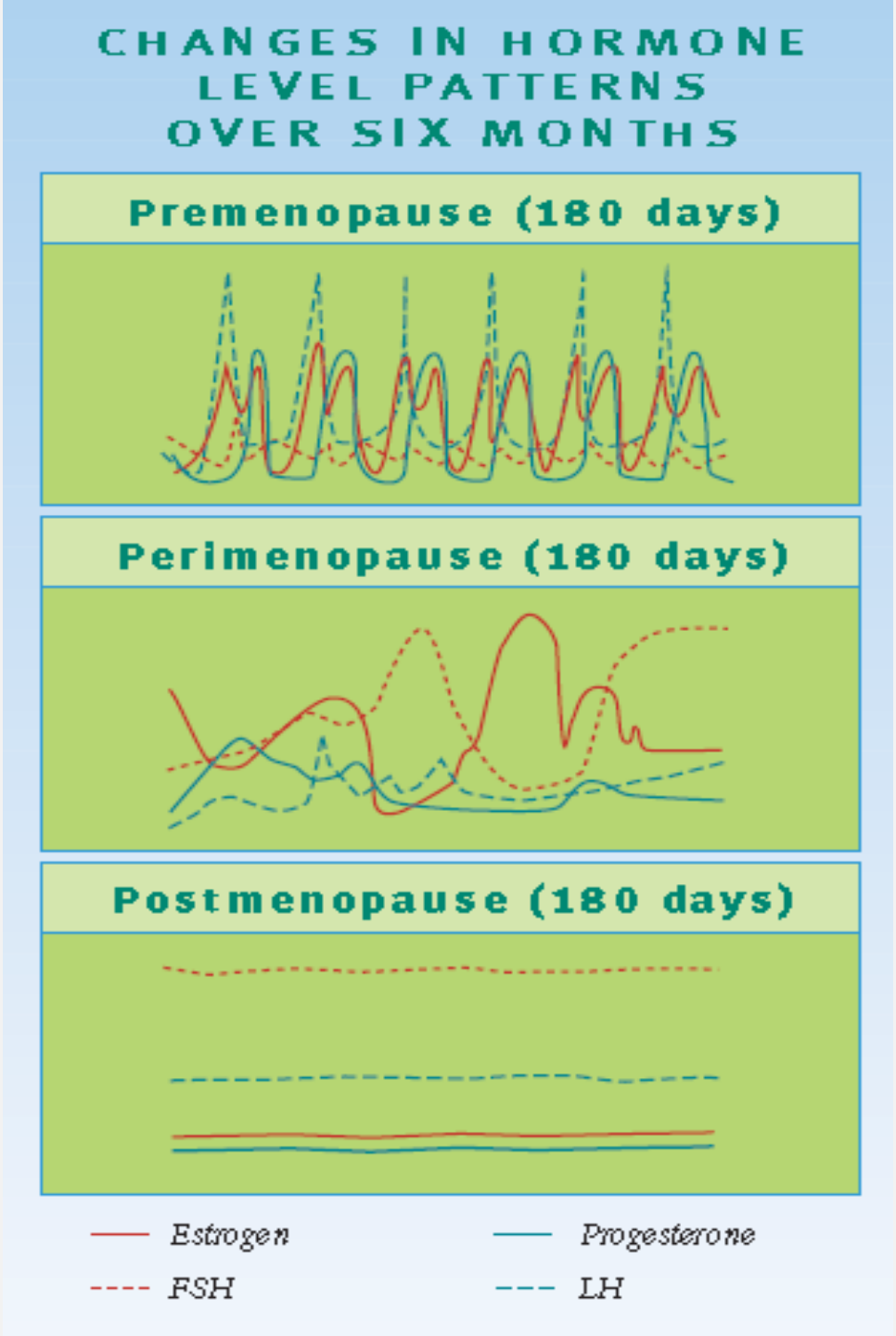


Figure 1 shows line drawings of about a **month** of estrogen levels during the menstruating years (premenopause), when cycles and experiences are changing in perimenopause, and during menopause that starts a year after the final menstrual flow.

- *Center for Menstrual Cycle and Ovulation Research CeMCOR at UBC*



Physiology of the Menopause Transition

Early Menopause Transition

- Persistent cycle irregularity by ≥7 d.
- Decline in inhibin B and AMH because of reduction in follicles (low AFC).
- Diminished ovarian reserve. Lower AMH and inhibin B promotes growth of remaining follicular pool, accelerating follicular atresia.
- Early follicular FSH is variable.
- Luteal out-of-phase (LOOP) events occur in about one in four cycles.
- May or may not have mild vasomotor symptoms (VMS).
- May have pronounced premenstrual syndrome.

Late Menopause Transition

- Amenorrhea > 60 d.
- Menstrual cycles have variable cycle length.
- Variable estradiol levels with increased prevalence of anovulation.
- FSH levels are ≥25 IU/L because of few remaining oocytes.
- Negligible AMH and AFC.
- LOOP cycles occur in a third of women; VMS and other signs of menopause likely.

LOOP events lead to symptoms of elevated estradiol

- Mastalgia, Migraine, Menorrhagia, Growth of fibroids, Endometrial hyperplasia
- Increased risk of reproductive cancers (especially with longer MT).
- Pregnancy can occur, with increased incidence of twins

Assessment - Lab Testing



- Serum hormone levels generally not recommended to guide treatment but may help in some cases in initial assessments for reproductive stage

- Consider FSH, LH, estradiol, testosterone, prolactin, TSH, AMH, genetic testing and endometrial biopsy
  - Age < 40, amenorrheic, fertility concerns
  - unable to assess bleeding status due to IUD or Hysterectomy/endometrial ablation
  - Atypical presentation of VMS or sx to rule out other etiologies (Thyroid dysfunction, infections, malignancy, pheochromocytoma, and carcinoid syndrome)

- Consider appropriate rheumatologic, endocrine labs, etc for atypical MSK, Genitourinary, Dermatologic, cognitive/mood, and constitutional symptoms

Measures of ovarian reserve

- FSH and E2 (days 2-5 of menstrual cycle, not taking hormones).
- Most common for measuring ovarian reserve.
- Low ovarian reserve if:

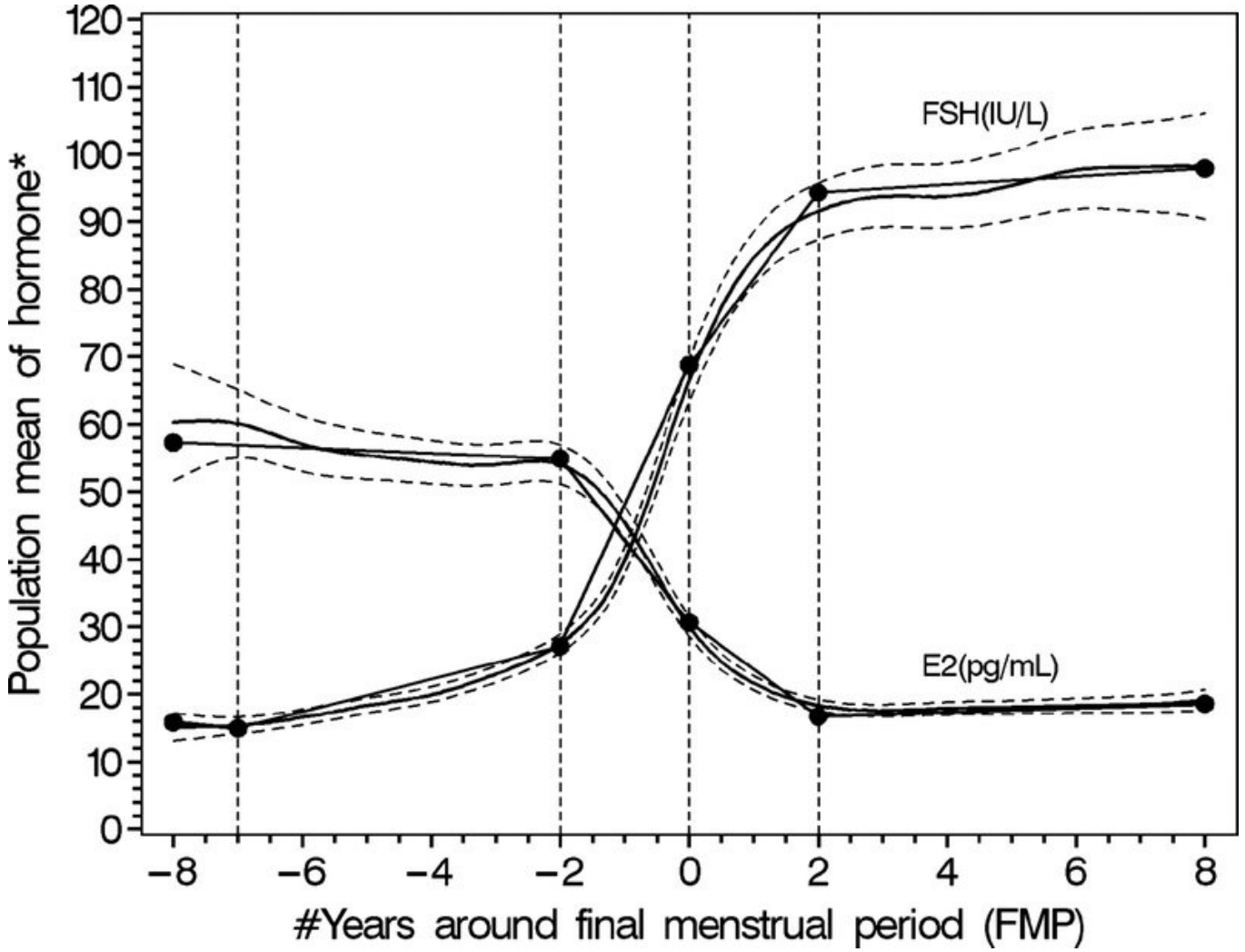
  FSH>10-15 IU/L and E2<60pg/mL

  FSH<10/L and E2>100 pg/ml (high E2 suppressing FSH)

- Not for general screening but useful markers of ovarian response to controlled ovarian stim

  AMH <1ng/mL

  AFC <7 follicles



Menopause Transition Scale

Please circle the answer that is closest to how you have felt in the last 2 wk.

SYMPTOM	EASY (3)	MODERATE (2)	HARD (1)
Hot Flashes/ Night Sweats	Rare to none, no sweating, predictable, barely distracting	Somewhat frequent, sweating, predictable, somewhat distracted from activity	Frequent, sweating, unpredictable, very distracting from activity
Weight	Stable, healthy or overweight, losing	Overweight or not losing	Obese or gaining
Energy	Good, rested in AM, mostly good days	Moderate, mostly rested in AM, good and bad days	Tired, mostly not rested in AM, mostly bad days
Libido	Both partners initiate, both satisfied, relationship good predictable, no dysfunction	Only partner initiates, OK once going, relationship mostly OK	No one initiating, no desire, relationship stressed
Moods	Good mood-rare mild anxiety/ depressed mood, no one notices,	Some anxiety/depressed mood, others notice, not predictable, some dysfunction	Mostly anxious or depressed, others notice, not predictable, poor function in daily activities
Vaginal Dryness	Minor to no dryness, rare to no bladder symptoms, no pain with intercourse	Some dryness, some bladder symptoms, mild pain with intercourse	Mostly dryness, always bladder symptoms, mostly pain with intercourse
Vaginal Bleeding	None or light, predictable, not interfering with daily activities	Moderate to heavy, predictable, some interference with daily activities	Heavy, not predictable, interfering with daily activities

Predominant Symptoms of MT and Menopause



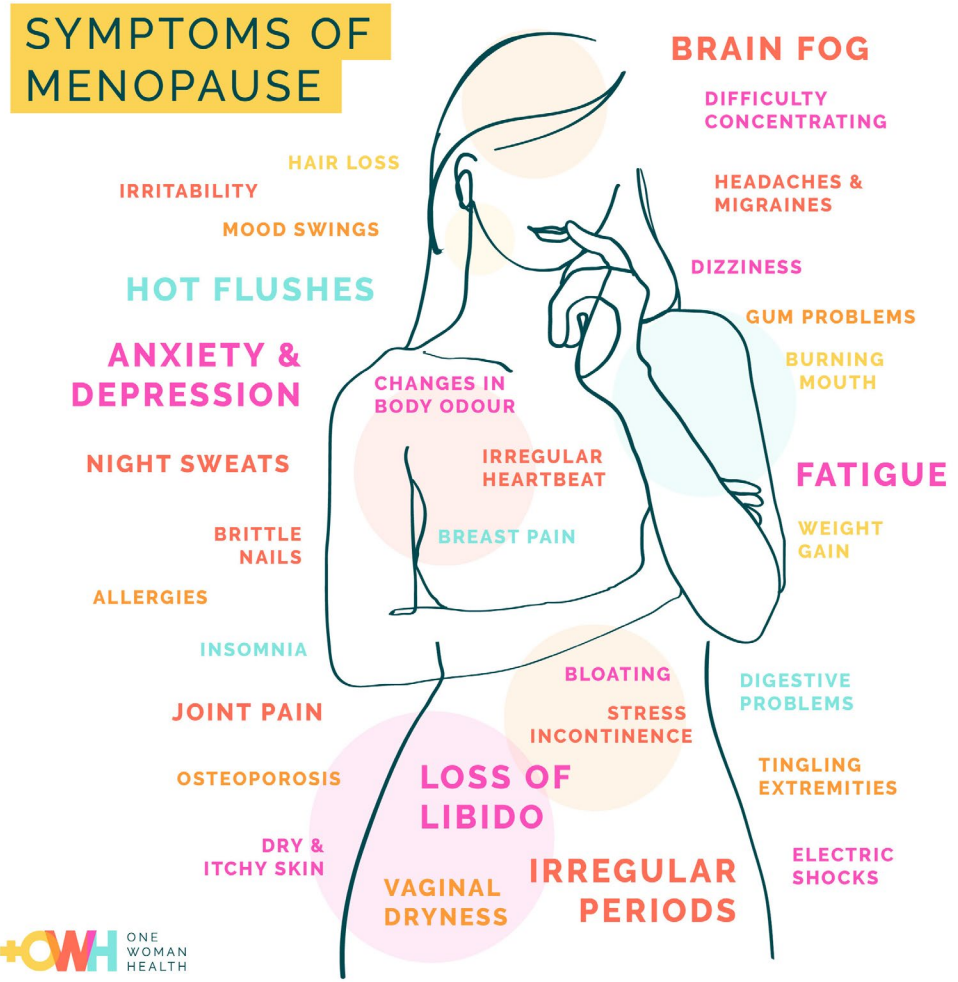
- **Vasomotor Symptoms - 80%**
  - Characterized by sudden intense heat in upper body lasting 30 sec to 5 min.
  - Often accompanied by perspiration, chills, anxiety, palpitations.
  - median duration 7.4 yrs (4.5 -20+ yrs)

- **Genitourinary Syndrome 40-50%**
  - Vaginal dryness, itching burning irritation discharge; dyspareunia, decreased arousal, delayed orgasm, post coital bleeding
  - Dysuria, nocturia, frequency, recurrent UTIs, incontinence

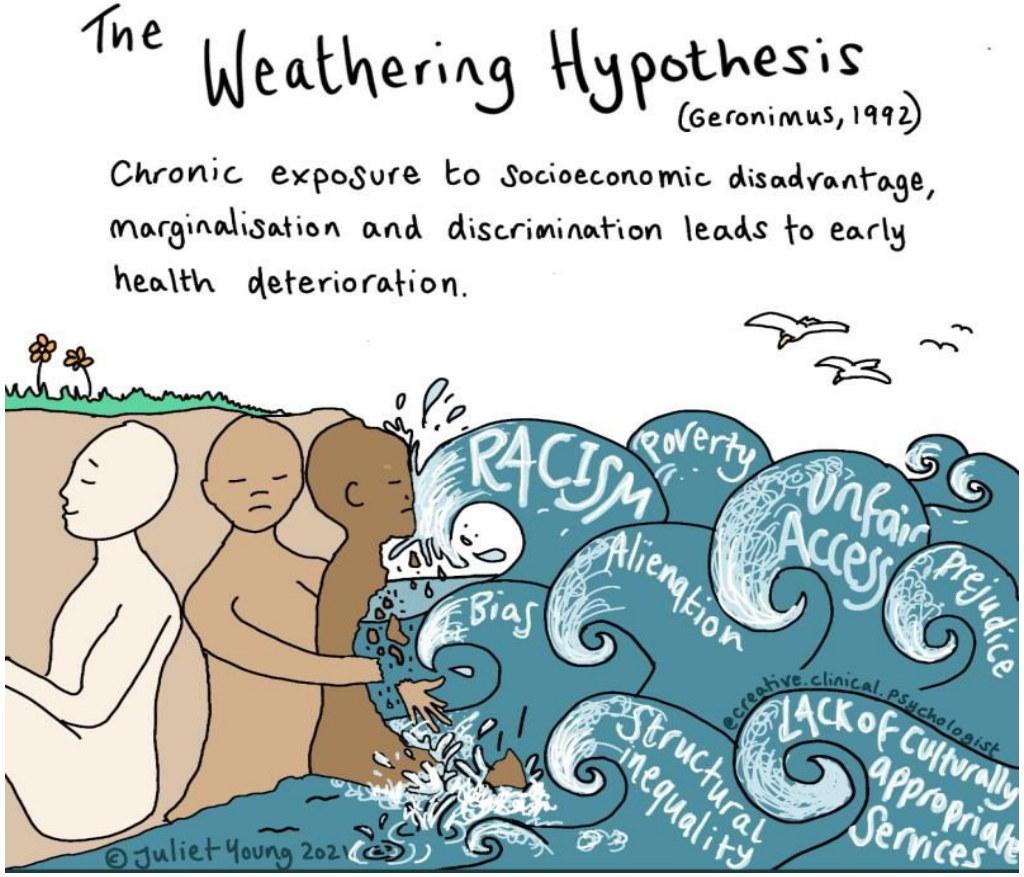
- **Musculoskeletal syndrome – 50%**
  - Arthralgia, arthritis, tendonitis (glut and shoulder), frozen shoulder, plantar fasciitis.
  - Rapid bone density loss in the first 5 years after LMP, leading to osteoporosis and problems with dental health

Menopause transition effects the whole body

- Sleep disruption 45%, Highest rates of sleeplessness in late perimenopause (45%) or surgical menopause (47%). Exacerbates nearly all other MT symptoms
- Mood changes 40-70% ~2 fold increase in depressive sx
- Cognitive changes ~40-62%: forgetfulness, word recall, info retrieval, concentration (learning and responding to info least affected)
- Skin and hair changes 30% decline in skin collagen in 1st 5 yrs of menopause about 2%/yr over the next 20
- Vision changes macular degeneration and glaucoma
- Weight gain central adiposity decrease lean mass
- Headaches or migraines variable E2 exacerbates,
- Decreased libido and sexual dysfunction



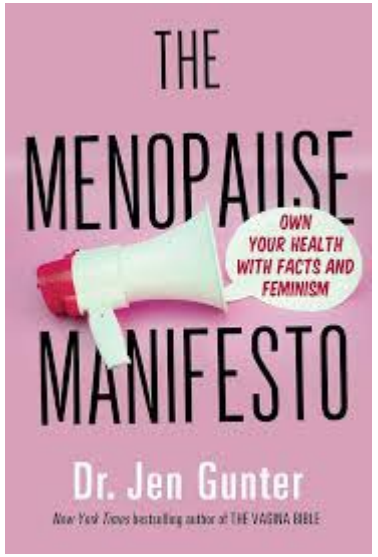
Social determinants of health may lead to greater intensity and duration of symptoms during MT, as well risk and benefit of treatment

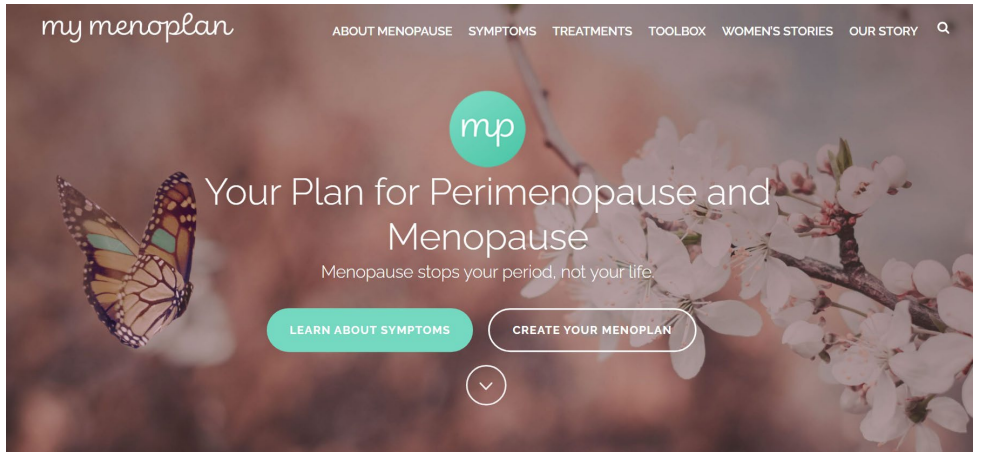


- Median duration of VMS of 7.4 years centered around FMP (SWAN) but may continue for 10 years or more:
  - African American women (10.1 y)
  - Hispanic women (8.9 y)
  - Non-Hispanic White women (6.5 y)
  - Chinese women (5.4 y)
  - Japanese women (4.8 y)
- Risk Factors for VMS include; low SES, low education attainment, Race or ethnicity, smoking, obesity or weight gain, high anxiety levels, oophorectomy, medical comorbidities (DM, OSA, Chronic pain conditions, thyroid disease)
- Earlier onset of menopause, depression, anxiety, stress, less college education, financial strain, single, smoker, poor social situation, and BMI greater than 30 kg/m^2 are **associated with longer duration of symptoms.**

Resources for patients (and you too)







https://healthy.kaiserpermanente.org/health-wellness/health-encyclopedia/he.menopause-and-perimenopause.hw228763

https://mymenoplan.org/

https://menopause.org/patient-education/menopause-topics/perimenopause

https://drjengunter.com/the-menopause-manifesto/

The Menopause Society™

Leading the Conversation

Home > Patient Education > Menopause Topics > **Perimenopause**

Resources for clinicians

American College of Obstetrics and Gynecology

American Academy Family Physicians

You can become a member of The Menopause Society to access position statements and educational material and Menopause journal.

ISSWSH – International Society for the Study of Women's Sexual Health

The American Society for Reproductive Medicine guidelines

References

Menopause Society; Menopause A-Z Slides 2024

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Richard-Davis G, et al. *JAMA Intern Med* 2015;175:540-541. doi: 10.1001/jamainternmed.2014.8099

Specialty Society Guidelines

ACOG: **Management of Menopausal Symptoms (2014, updated 2024)**

TMS: **Nonhormone Therapy Position Statement (2023)**

TMS: **Hormone Therapy Position Statement (2022)**

TMS: **Genitourinary Syndrome of Menopause Position Statement (2020)**

NICE: **Menopause: identification and management (2015, updated 2026)**

IMS: **Recommendations and Key Messages on Women's Midlife Health and Menopause**

MHT OPTIONS, RISKS, BENEFITS & INDIVIDUALIZED TREATMENT PLANS



SEPT 24, 2026

Mary Beth Welch, MD, MSCP
KP Bellevue OB-GYN

THE PERFECT CANDIDATES



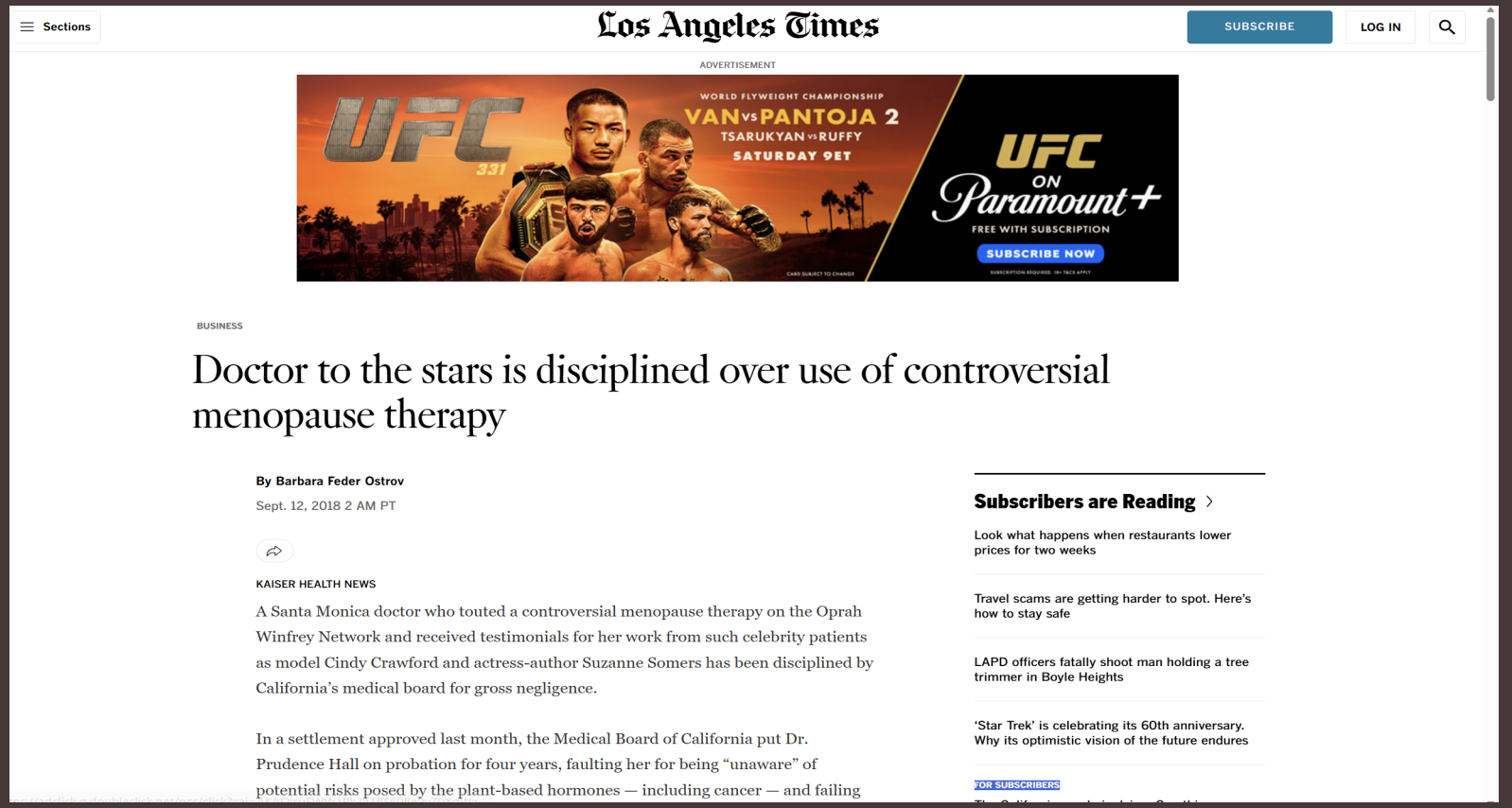


WHAT DO WE DO WITH EVERYONE ELSE?

DO WE GO WITH THE INFLUENCERS?



DO WE GET SCARED OF LAWSUITS BROUGHT BY PATIENTS OR THEIR HEIRS?



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Los Angeles Times

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BUSINESS

Doctor to the stars is disciplined over use of controversial menopause therapy

By Barbara Feder Ostrov

Sept. 12, 2018 2 AM PT

KAISER HEALTH NEWS

A Santa Monica doctor who touted a controversial menopause therapy on the Oprah Winfrey Network and received testimonials for her work from such celebrity patients as model Cindy Crawford and actress-author Suzanne Somers has been disciplined by California's medical board for gross negligence.

In a settlement approved last month, the Medical Board of California put Dr. Prudence Hall on probation for four years, faulting her for being "unaware" of potential risks posed by the plant-based hormones — including cancer — and failing

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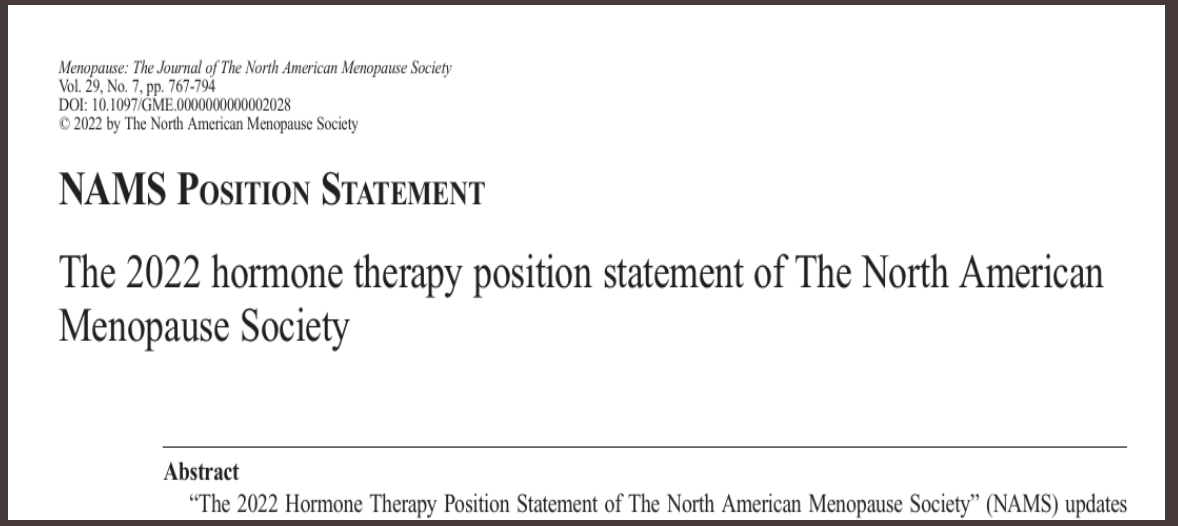
MHT…FOR THE "NON IDEAL" CANDIDATE?

Contraindications: relative and absolute

Additional considerations if you are going to prescribe to patient with:

- Personal history of breast cancer
- Personal history of gynecologic cancer
- Personal h/o CVD/CVA
- Personal h/o VTE or thrombophilia
- Age >60 or >10 years since LMP

MENOPAUSE SOCIETY/NAMS GUIDELINES



Menopause: The Journal of The North American Menopause Society
Vol. 29, No. 7, pp. 767-794
DOI: 10.1097/GME.0000000000002028
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NAMS Position Statement

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

Abstract

"The 2022 Hormone Therapy Position Statement of The North American Menopause Society" (NAMS) updates

- UNEXPLAINED VAGINAL BLEEDING
- LIVER DISEASE
- PRIOR ESTROGEN-SENSITIVE CANCER
- PRIOR CORONARY HEART DISEASE, STROKE, OR MI
- PRIOR VTE
- HIGH RISK OF THROMBOEMBOLIC DISEASE

NON-HORMONAL THERAPIES ARE FIRST LINE IN PATIENTS WITH THESE CONDITIONS

NOT INCLUDED…AND WHAT I WOULD WANT:

STRONG FAMILY HISTORY OF…

Breast cancer……genetic testing, chemoprevention, prophylactic surgery

Early MI…….phone a PCP friend

Blood clot…….genetic testing

NOT CONTRAINDICATIONS IN AND OF THEMSELVES...

Smoking

Migraine with aura

High cholesterol

Weight/BMI

HTN

DM

H/o endometriosis (use E+ P even if s/p hysterectomy)

DISCLAIMER: THESE APPROACHES ARE A COMPILATION OF (REPUTABLE) SOURCES, AND ARE NOT NECESSARILY ENDORSED BY THE MENOPAUSE SOCIETY OR ME PERSONALLY

PERSONAL H/O BREAST CANCER

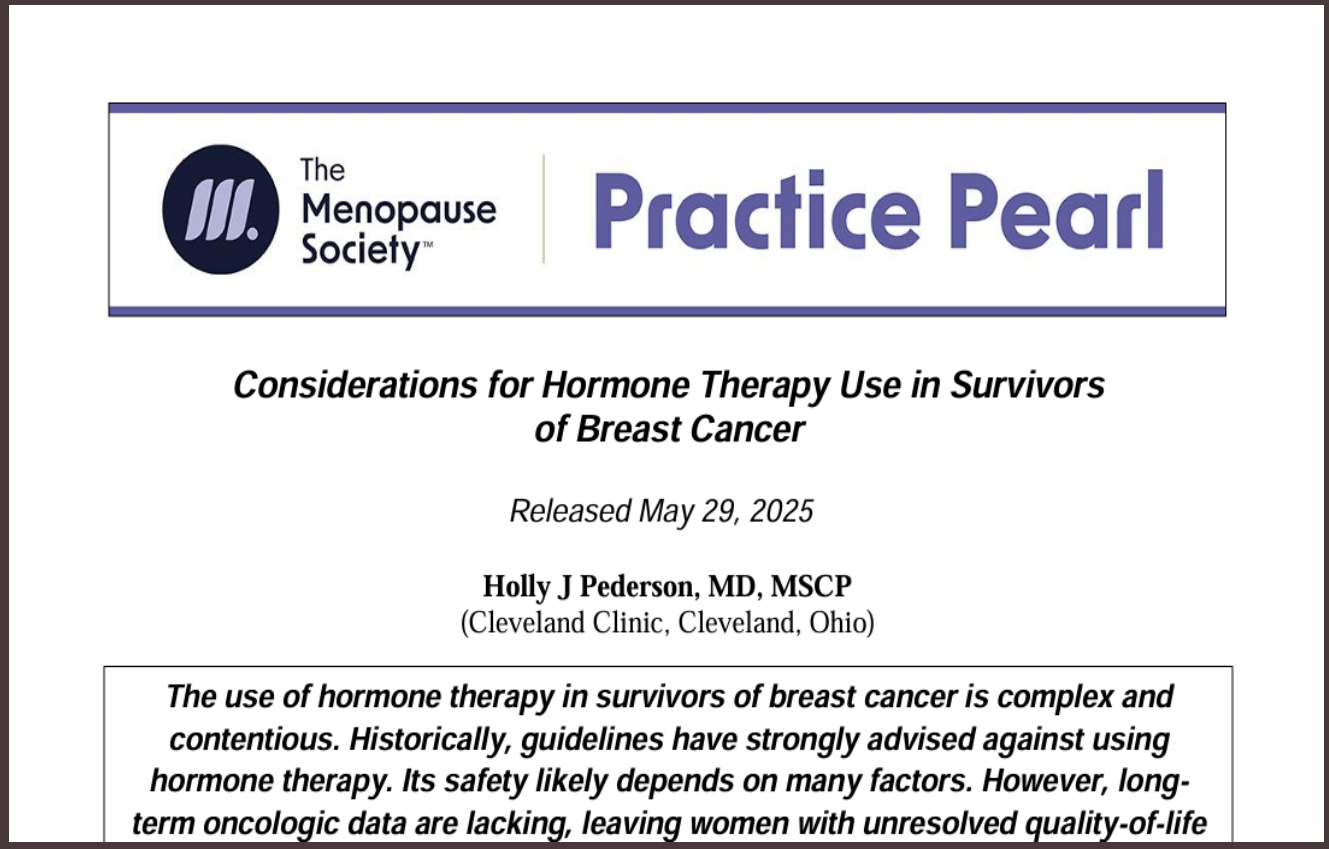
Must consider: tumor type, stage, recurrence likelihood, response to treatment, time since diagnosis, inherent risk of another cancer

Long term safety data lacking. Studies are old. Preparations and treatments have changed

HABITS trial: increased risk of breast cancer events but no increased metastasis or death

If you do: for ER receptor negative, after 5 years

DCIS: Promise Study. Duavee? Premarin + Bazedoxifene



The Menopause Society™ | Practice Pearl

Considerations for Hormone Therapy Use in Survivors of Breast Cancer

Released May 29, 2025

Holly J Pederson, MD, MSCP
(Cleveland Clinic, Cleveland, Ohio)

The use of hormone therapy in survivors of breast cancer is complex and contentious. Historically, guidelines have strongly advised against using hormone therapy. Its safety likely depends on many factors. However, long-term oncologic data are lacking, leaving women with unresolved quality-of-life

Partner with medical oncologist

HISTORY OF GYN CANCER: IT DEPENDS ON TYPE

Cervical: OK

Uterine: Not recommended with advanced stage endometrial and uterine sarcoma

Ovary: Not recommended with low grade serous and endometrioid ovarian cancer

OK for Lynch/BRCA carriers after BSO if no personal h/o cancer



CLINICAL PRACTICE STATEMENT · Volume 157, Issue 2, P303-306, May 2020 Download Full Issue

Hormone therapy (HT) in women with gynecologic cancers and in women at high risk for developing a gynecologic cancer: A Society of Gynecologic Oncology (SGO) clinical practice statement

This practice statement has been endorsed by The North American Menopause Society

A.K. Sinno [a] · J. Pinkerton [b] · T. Febbraro [c] · ... · S. Temkin [f] · D. Iglesias [g] · B. Pothuri [h] ... Show more

Affiliations & Notes Article Info

Partner with Gynecologic Oncologist

CVD: CAD, H/O MI, H/O CVA, HEART FAILURE, PAD

Indication?

Risks/benefits

If you do: Low dose/transdermal

Stop if not effective

Partner with PCP/Cardiology

Circulation
Volume 147, Issue 7, 14 February 2023; Pages 597-610
https://doi.org/10.1161/CIRCULATIONAHA.122.061559

IN DEPTH

Rethinking Menopausal Hormone Therapy: For Whom, What, When, and How Long?

Leslie Cho, MD, Andrew M. Kaunitz, MD, Stephanie S. Faubion, MD, MBA, Sharonne N. Hayes, MD, Emily S. Lau, MD, MPH, Nicole Pristera, MD, Nandita Scott, MD, Jan L. Shifren, MD, Chrisandra L. Shufelt, MD, MS, Cynthia A. Stuenkel, MD, and Kathryn J. Lindley, MD for the ACC CVD in Women Committee

	ASCVD SCORE	MHT Recommendations
Low Risk	< 5%	No restrictions
Intermediate Risk	5-10%	Transdermal only
High Risk	> 10%	Not recommended

H/O VTE OR CLOTTING DISORDER

Indication?

Other factors increasing clot risk? Other contraindications? On lifetime anticoagulation?

Provocation and vessel damage

PE, brain clot - no

Heterozygous gene mutation probably OK per Endocrine Society – one study of 100 patients

If you do: Transdermal estradiol, max 0.05 mg, micronized progesterone or Mirena for progestogen

Partner with Hematology

Estrogen and the Risk of Blood Clots with Menopausal Hormone Therapy

Ask Dr. Jen



DR. JEN GUNTER

APR 09, 2023 · PAID

AGE > 60 OR >10 YEARS SINCE LMP

Indication?

Otherwise an ideal candidate? – ASCVD, cardiac calcium score, other lipid testing

Increase in CVD, stroke and VTE (age 60) and dementia risk (age 65) using WHI preparations

Mixed data using modern preparations

If you do: transdermal estrogen only, start low with 0.025 weekly patch

Stop if not effective

HORMONE THERAPY GUIDE

Age and Starting Menopausal Hormone Therapy

Risks and Recommendations



DR. JEN GUNTER

AUG 27, 2023 · PAID

NO RX FOR SYSTEMIC MHT?

DON'T FORGET:

Optimize lifestyle for longevity/brain health/CV

Bone health: candidate for early DEXA?

Musculoskeletal syndrome of menopause: PT, weight mgmt

GSM: Topical vaginal estrogen

VMS non hormonal options:

---Neurokinin B antagonist: Fezolinetant (Veozah) and Elinzanetant (Lynkuet)

---SSRI/SNRI (Paroxitine 7.5 =Brisdelle)

--Gabapentin

--Oxybutynin?

HSDD: Flibanserin (Addyi) orTestosterone?

Sleep: need for sleep study?, CBT-I

THANK YOU!



MENOPAUSE

Prescribing HRT with Confidence:

Pharmacology, Formulary tools, and practical pearls

Menopause/Perimenopause for Primary Care • Sept 24, 2026

Galen Goertzen, PharmD, BCACP
Pharmacy specialty coordinator

Kaiser Permanente Washington

Objectives

- Compare pharmacology of oral vs transdermal estrogen, and micronized vs synthetic progestins.
- Demonstrate SmartRx and formulary tools to identify covered options, cost-effective choices, and prior authorization pitfalls.
- Evaluate common supplements marketed for menopause: evidence, safety, and counseling strategies.
- Introduce compounding basics: when it’s appropriate, regulatory considerations, and how to counsel patients about risks.

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Reframing the WHI

What the landmark trial showed, what it did not answer, and why formulation and age matter.

Galen Goertzen

Conclusions of the WHI

Conclusions Overall health risks exceeded benefits from use of combined estrogen plus progestin for an average 5.2-year follow-up among healthy postmenopausal US women. All-cause mortality was not affected during the trial. The risk-benefit profile found in this trial is not consistent with the requirements for a viable intervention for primary prevention of chronic diseases, and the results indicate that this regimen should not be initiated or continued for primary prevention of CHD.

WHI investigators *JAMA* 2002;288(3):321-33

WHY BROAD INTERPRETATION OF WHI IS LIMITED

Three key factors limit the generalizability of Women's Health Initiative (WHI) findings to today's menopausal hormone therapy (MHT) care.

1 OLDER STUDY POPULATION

Average age at screening

63.2 YEARS

~10 years older than the typical age of menopause onset (51–52 years)

Why this matters

- Older women have higher baseline risks of CVD, stroke, VTE, and breast cancer.
- Risks and benefits of MHT differ by age and time since menopause.
- WHI was not powered for age-specific subgroup analyses.

→ Findings in women in their 60s+ cannot be assumed to apply to younger, recently menopausal women.

2 SPECIFIC FORMULATION USED: CEE + MPA

Estrogen:
Conjugated equine estrogen (CEE)

Progestogen:
Medroxyprogesterone acetate (MPA)

Why this matters

- CEE contains multiple estrogens (and unique equine estrogens) with receptor activity different from estradiol.
- CEE appears to be more proinflammatory and less favorable for lipid and vascular effects.
- MPA has androgenic and glucocorticoid activity and may increase insulin resistance.

→ **Results with CEE + MPA cannot be assumed to apply to estradiol with micronized progesterone.**

3 ORAL ROUTE IN WHI VS TRANSDERMAL ROUTE

WHI Route
Oral

First-pass hepatic metabolism

Alternative Route
Transdermal

Bypasses first-pass hepatic metabolism

Why this matters

- Oral estrogen increases hepatic production of clotting factors, CRP, and triglycerides.
- Transdermal estrogen has minimal impact on hepatic proteins and triglycerides.
- Lower VTE and stroke risk with transdermal estrogen compared with oral estrogen.

→ **Route of administration materially influences risk profile and should be part of individualized MHT decisions.**

CLINICAL IMPLICATION

The WHI provides important information, but its findings cannot be broadly extrapolated.

Modern MHT decisions should consider:

- Patient age and time since menopause
- Hormone formulation (estradiol + micronized progesterone preferred)
- Route of administration (transdermal preferred for many patients)
- Individual risk profile and treatment goals

Context matters. Formulation matters. Route matters. Individualization matters.

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Conjugated equine estrogen versus estradiol-17B

- Some estrogen that occur in horses do not occur in humans
- There are two unique estrogen receptors, α and β, which were cloned in 1996. Estradiol binds equally to α and β, while CEE favors the β receptors.
- CEE is far more active in increasing inflammatory markers C-reactive protein and inducing matrix metalloproteinase 9



Yasar P et al. *Reprod Med Biol* 2016:16-4-20
Berrodin TJ et al. *Mol Endocrinol* 2009;23:74-85

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Medroxyprogesterone Acetate vs Micronized Progesterone

Clinical Comparison

	Medroxyprogesterone acetate	Micronized Progesterone
Receptor activity	• Binds to progesterone receptors • Binds to androgen and glucocorticoid receptors	• Binds to progesterone receptors with high affinity and selectivity • Minimal binding to androgen or glucocorticoid receptors
Metabolic	• Increased insulin-like growth factor • Increased insulin resistance	• Neutral effect on IGF=1 • No increase in insulin resistance seen
Safety	Associated with: • Increased risk of VTE • Increased risk of breast cancer • Less favorable cardiometabolic components	No association shown with: • Thromboembolic risk • Higher incidence of breast cancer • Adverse cardiometabolic effects
Peanut allergy	• No known peanut-derived components	• Cannot be used in patients with peanut allergies

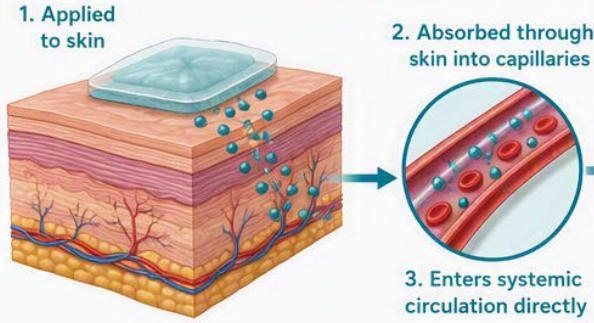
TRANSDERMAL vs ORAL ESTRADIOL

Route Matters. Different Journey. Different Impact.

TRANSDERMAL ESTRADIOL

Bypasses liver first pass

THE JOURNEY



SYSTEMIC CIRCULATION

Consistent delivery to tissues

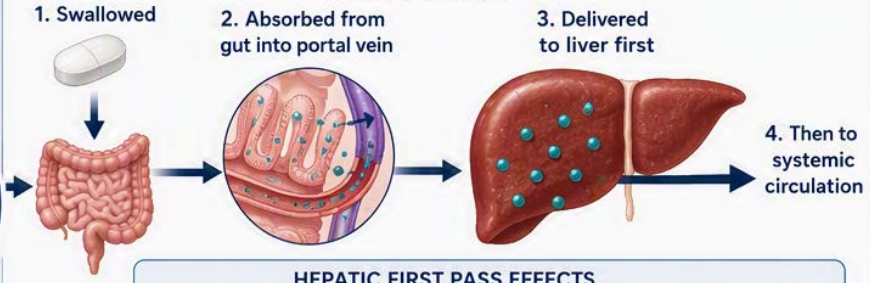
BYPASSES LIVER FIRST PASS

Delivers estradiol directly to systemic circulation, avoiding initial hepatic metabolism.

ORAL ESTRADIOL

Undergoes liver first pass

THE JOURNEY



HEPATIC FIRST PASS EFFECTS

Hepatic Proteins	Clotting Factors	Triglycerides	CRP
• SHBG • Angiotensinogen • IGF-1	• Fibrinogen ↑ • Factors VII, VIII, IX, X ↑		C-Reactive Protein

Increased hepatic protein synthesis can elevate risk markers for thrombosis and cardiovascular events.

TRANSDERMAL ESTRADIOL – KEY BENEFITS

Minimizes impact on liver protein synthesis

Lower effect on clotting factors, triglycerides, and CRP

More stable blood levels

Avoids peaks and troughs associated with oral dosing

Potentially lower risk

Lower VTE risk compared with oral estrogen

IDEAL FOR: Women with elevated VTE risk, hypertriglyceridemia, metabolic syndrome, liver concerns, or inflammatory conditions.

BLOOD LEVEL STABILITY



Transdermal provides steadier estradiol levels; oral dosing results in peaks and troughs.

ORAL ESTRADIOL – CLINICAL CONSIDERATIONS

Increases hepatic protein synthesis

May raise clotting factors, triglycerides, and CRP

Greater metabolic impact

May influence lipid profile and inflammation

Higher VTE risk

Associated with increased thromboembolic risk compared with transdermal estrogen

USE WITH CAUTION: History of VTE, hypertriglyceridemia, liver disease, metabolic syndrome, or inflammatory states.

CLINICAL PEARL

Route of estrogen delivery significantly influences safety profile. Transdermal estradiol delivers effective symptom relief while minimizing hepatic stimulation and associated risks.

BOTTOM LINE

Transdermal = Direct. Stable. Liver-sparing.
Oral = Indirect. Variable. Liver-stimulating.

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Key comparison: transdermal vs oral estradiol

Effect	Transdermal estradiol	Oral estradiol
Absorption	Through skin	Through gut and liver
Entry into body	Directly into systemic circulation	After gut and liver metabolism
First-pass effect	Bypasses first pass	First pass
Estrogen	Remains mostly E2	Converts some E2 to E1
E2/E1 ratio	Higher E2, more physiologic	Lower E2:E1, less physiologic
Liver proteins + clotting factors	Less impact	Greater impact
Blood levels	More stable	Less stable

Title of presentation goes in this space

Greater hepatic effect increases production of clotting factors, SHBG, triglycerides, and CRP; higher oral doses may be needed to achieve the same estradiol-mediated benefit.

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So what do we have??

Strong physiological evidence

- Estradiol appears to be safer then conj estrogen
- Micronized progesterone appears to be safer than medroxyprogesterone acetate
- Transdermal route appears to be safer than oral route

Strong observational data

- WHI limited by age at enrollment
- Observational data consistent in showing transdermal biosimilar agents safer than oral conjugated estrogen and micronized progesterone safer than medroxyprogesterone

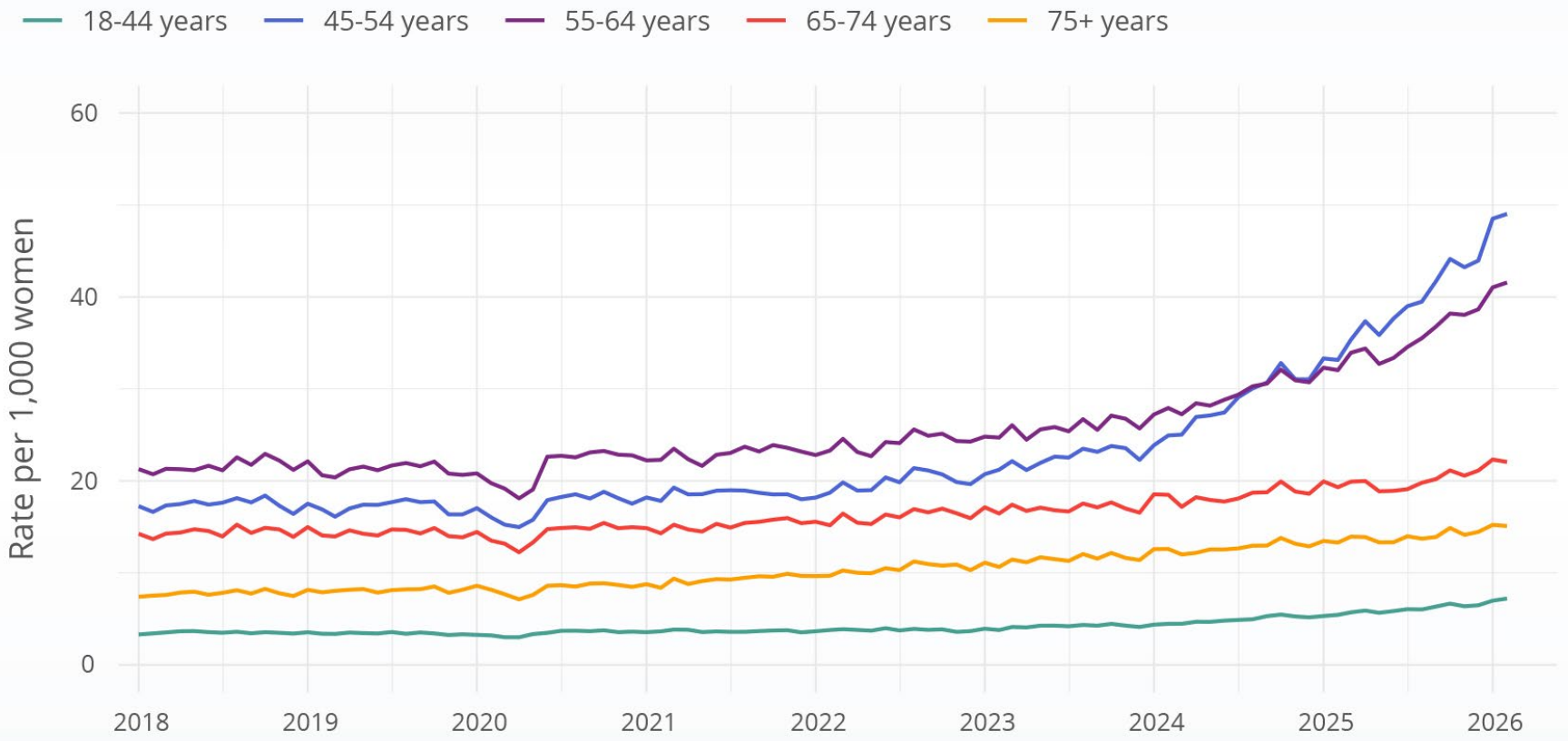
What don’t we have?

- Large randomized controlled trial - but do we need one??

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Estrogen-based hormone replacement therapy prescriptions per 1,000 women, by age group



"Estrogen-based hormone replacement therapy use is rising" 2026. Truveta.com.

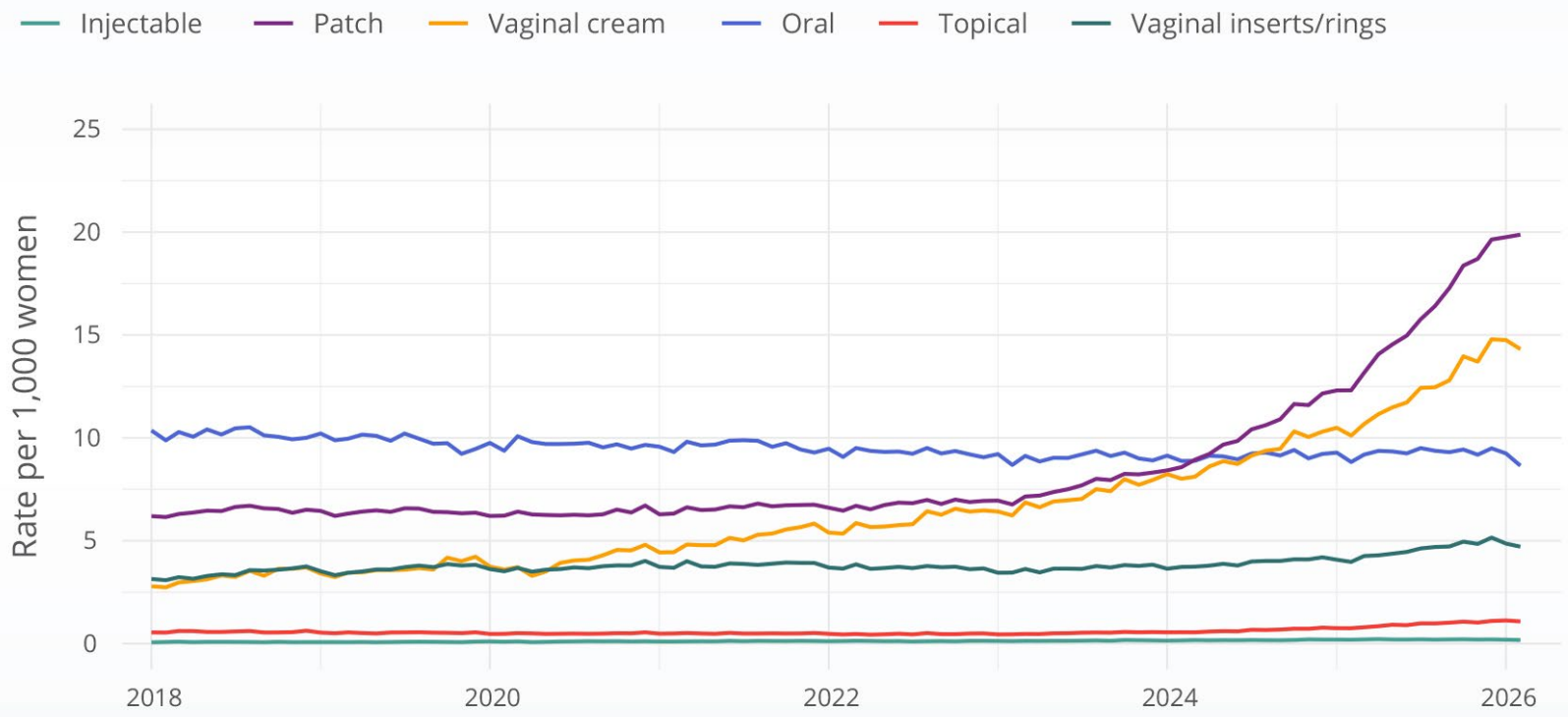
TRUVETA

[Truveta research](), April 9, 2026

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Estrogen-based hormone replacement therapy dispenses per 1,000 women by type



"Estrogen-based hormone replacement therapy use is rising" 2026. Truveta.com.

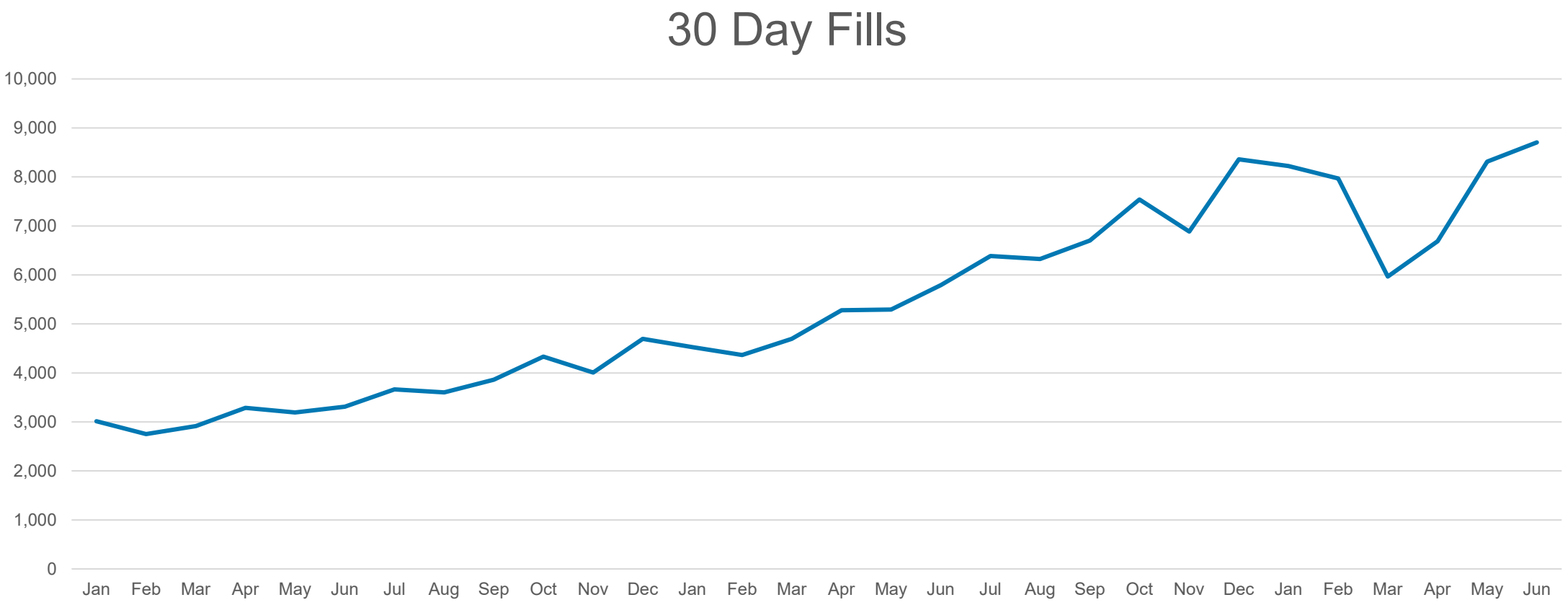
TRUVETA

[Truveta research](), April 9, 2026

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KPWA 30 day fills for estradiol patches Jan 2024 to June 2026



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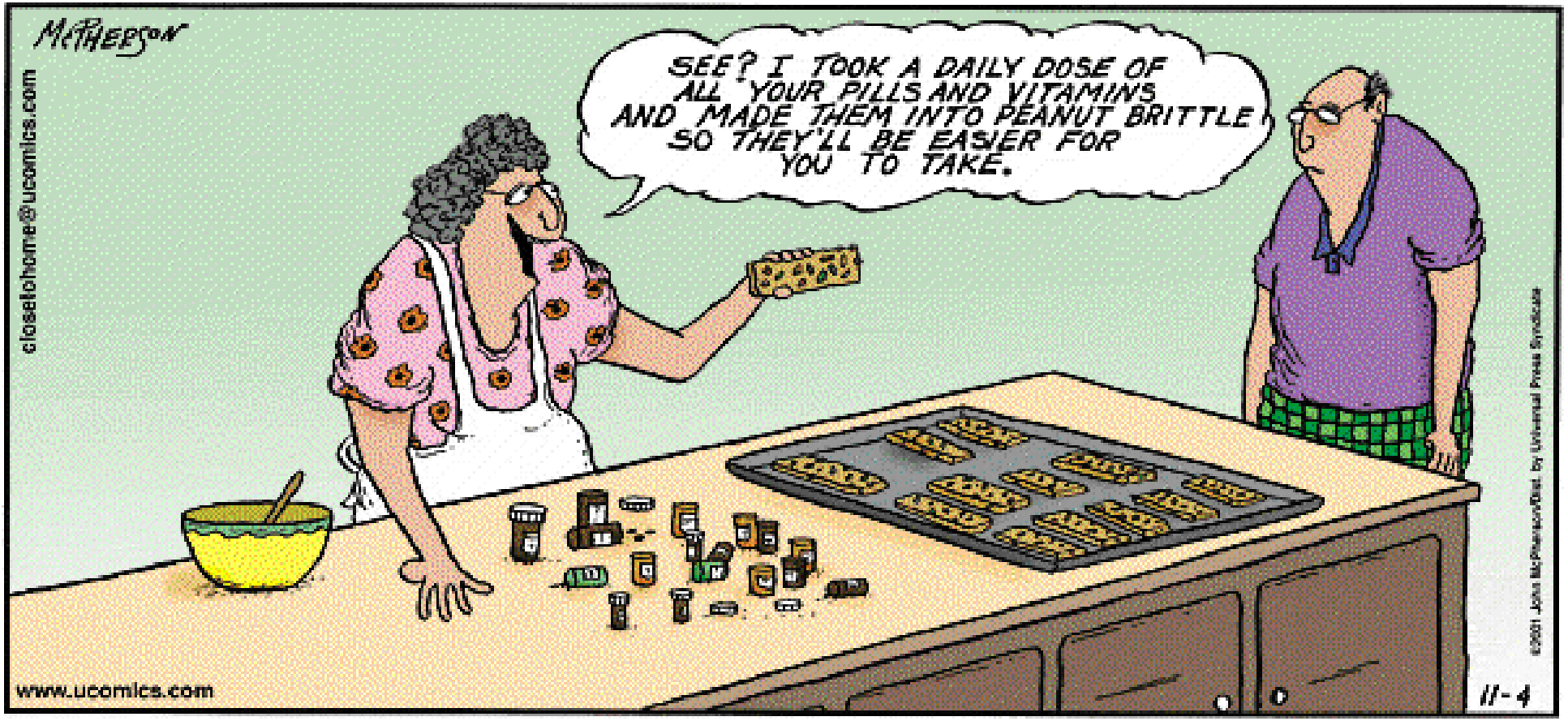
Patch shortage – expected to last through end of year

- **Increased demand:** removal of black box warning led to surge in prescriptions
- **Manufacturing limitations:** production of patches is complex with limited manufacturers
- **Supply chain delays:** Pharmacies order stock months in advance based on now outdated lower projections
- **Manufacturing issues:** Specific suppliers, including Sandoz and Amneal (preferred contract), have reported production issues.

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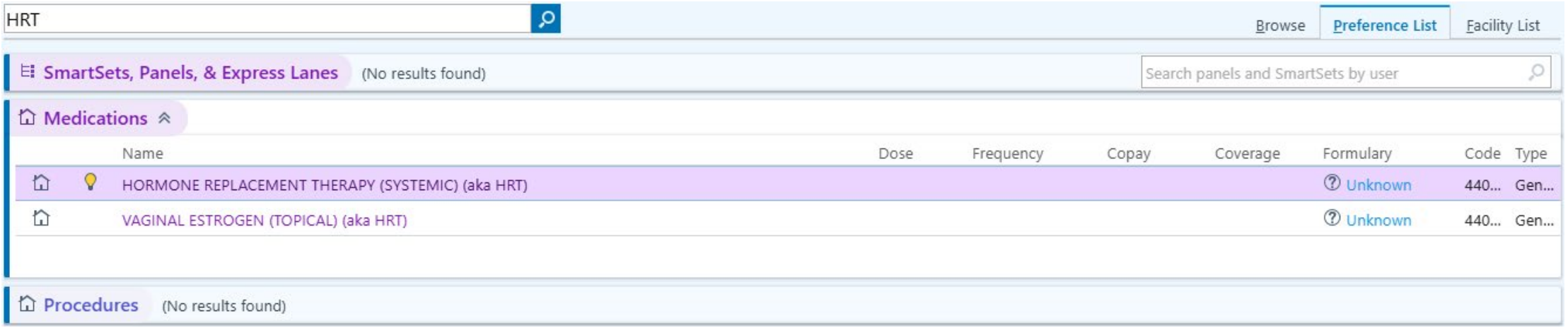
CLOSE TO HOME **BY JOHN McPHERSON**



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Prescribing HRT: Use the Smart Rx



Notes

- Good news – we now have a preferred contract on generic twice weekly Dotti
- Bad news - we can't get Dotti right now
- Micronized progesterone is preferred and available
- No preferred combination patches – only combination patch on the market (Combipatch) contains Norethindrone as progestin. Also still ***very*** expensive.

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Practicalities of using a patch – cutting patches

Climara and Dotti (plus associated generics) are “matrix” patches. Medication is evenly distributed throughout patch so they may be cut.

- Use sharp scissors
- If patch is circle fold in half and then cut on fold line
- If patch is oval cut along the perforation line.
- Store the remaining half in its original foil package and then in a sealed airtight container (i.e. Zip-lock)
- Store in a dry, room temperature location.

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Other tips for using estradiol patches

Problem #1 – patch is falling off

- Most common reason is water exposure so keeping it dry is important
- Apply a piece of Tegaderm over the patch to form a watertight seal

Problem #2 – reaction to adhesive

- Spray a little Flonase on the skin and let dry prior to application
- Apply a protective skin barrier (i.e. Cavilon NO Sting Barrier Film) between the skin and the adhesive
- Consider taking oral antihistamine (i.e. cetirizine) before applying the patch
- Cool the skin with an ice pack for 2-3 minutes before applying the patch.

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Complementary medicine

Medical News | WOMEN'S HEALTH

Wild West or Gold Rush: How Long-Neglected Menopause Care Has Spawned a Booming Marketplace

'ate Schweitzer

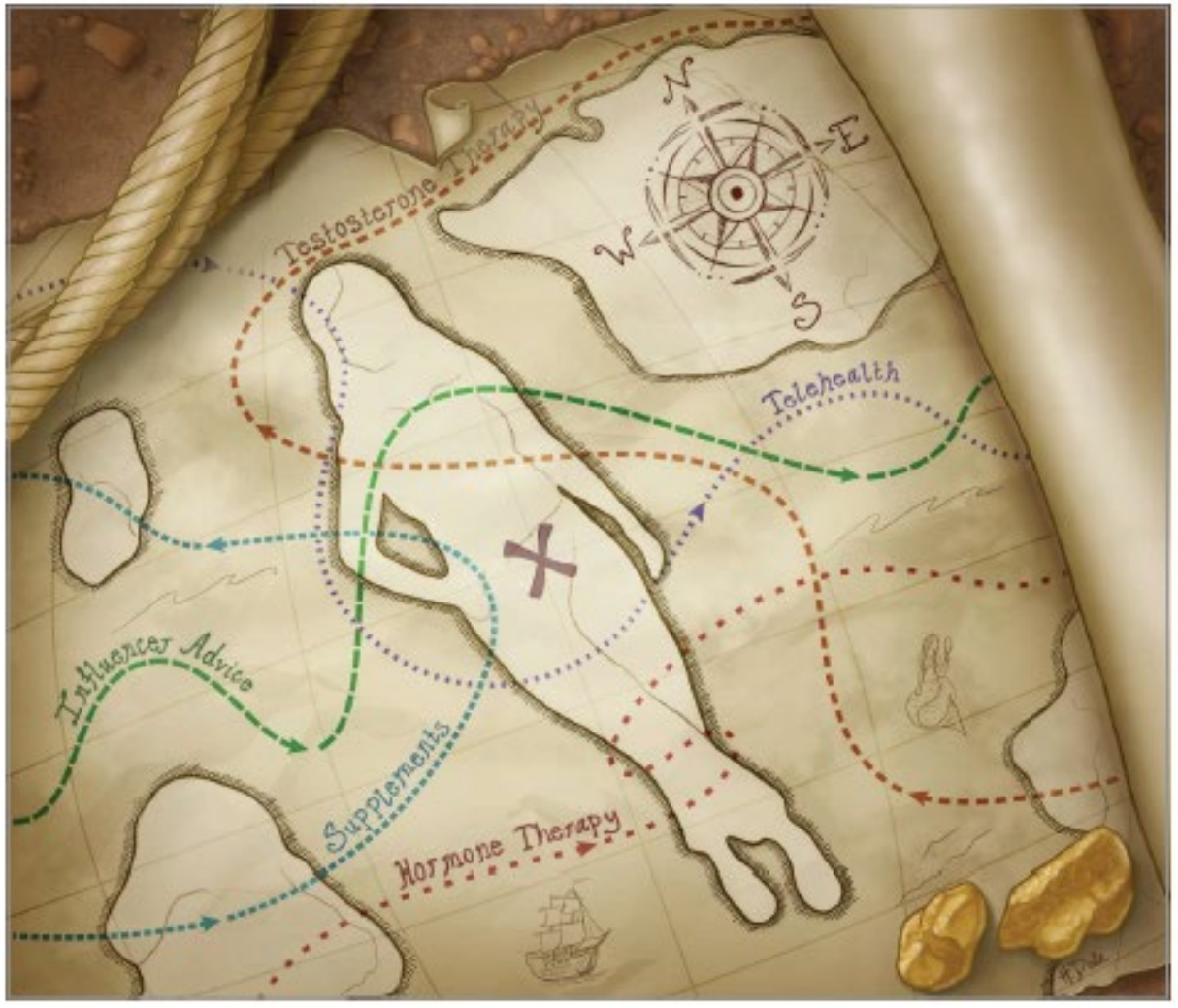
earch *menopause*, and there's no shortage of advice.

These days, social media feeds are ng with influencers touting their per- ested "hacks" to solving meno- ptoms and celebrities promot- upplements and skincare lines.

Telehealth compa- nies promise con- venient access to specialists while a growing number of startups market ned to ease hot flashes, im- estore libido, and sharpen

ebsite

seeking answers, this explo- and providers following de- epresents a long-overdue rush fueled by growing nand for better care. To attention has created a ndscape akin to the law-



Schweitzer K, JAMA 2026; 336(7)535-8

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Compounded Hormone Therapy (CHT)

Estimates (2015) that 1 to 2.5 million U.S. women aged 40 or older use compounded hormone therapy every year

26-33 million prescriptions annually - $1 up to $6 billion annually

Estimates - about 40% of hormonal therapy prescriptions are compounded

FDA does not have oversight of compounding pharmacies – State Board of Pharmacy – products are not FDA approved

Women have very little knowledge about safety concerns with their medications

Pinkerton JV et al. *Menopause* 2019;22(9):929-36

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What is “bio-identical”?

Marketing term per the FDA

Products that have same chemical structure as ones produced in human body include estradiol and micronized progesterone – both FDA approved formulary prescription products

FDA approved estradiol made from the same plant sources from which the base product of compounded estrogen products are made.

Difference: Rx products are regulated by the FDA to ensure they are safe and effective and contain the ingredients they are supposed to have, and NOT other active ingredients.

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Issues identified with compounded MHT

Inconsistency of content of compounded products

Possible increase in endometrial cancer due to higher estrogen and lower progesterone doses

Product contamination and impurities

Incomplete adverse event reporting and transparency

Lack of honest risk/benefit analysis (i.e. no package insert)

Unintentional transfer of cream to kids or pets

Checking blood levels is not helpful – titrate to symptom benefit

Cost - $40 - $250 per month – not including labs and consultation fees

Stuenkel CA et al. *JAMA Intern Med* 2021;181(3)370-1

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Compounding pharmacy variability

2019 study included capsule and cream formulations from 13 different compounding formulations

- Tested for actual content of estradiol and progesterone
- 11/13 pharmacies had levels +/- 10% of reported estradiol and progesterone concentration
- 2/13 in each group had variation from 26% below label to 31% above

Conclusion: “The variation in estradiol and progesterone levels observed in compounded HT formulations justify concerns regarding risks as a result of variability . . . . “

Stanyczyk FZ, et al. *Menopause*: 26(9): 966-71

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How to choose safe compounding pharmacy

Alliance for Pharmacy Compounding – advocacy organization

License – should be licensed with state board of pharmacy

Accreditation - Pharmacy Compounding Accreditation Board (PCAB) – search at ACHC.org

FDA public enforcement - check for inspections, recalls and other actions

Ask questions – process, training, quality standards

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Groups that recommend against regular use of compounded hormonal therapy

American College of Obstetricians and Gynecologists (ACOG)

National Academy of Sciences, Engineering, and Medicine (NASEM)

The Menopause Society

The Endocrine Society

Food and Drug Administration (FDA)

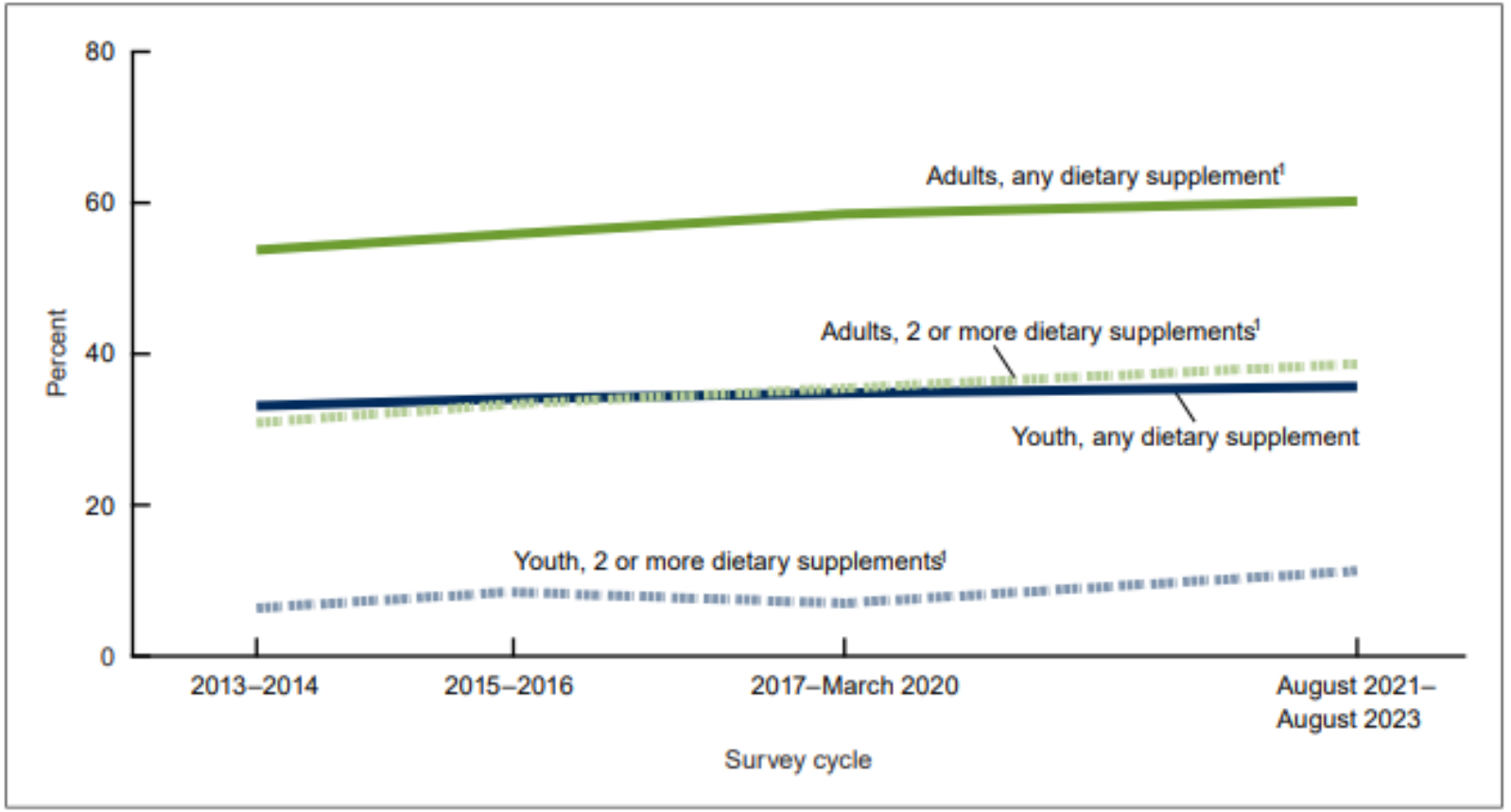
Kaiser Permanente Washington and National

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Dietary supplement use continues to rise (slowly)

Figure 4. Trends in percentage of youth and adults who used any dietary supplement or two or more dietary supplements in past 30 days: United States, 2013–2014 through August 2021–August 2023



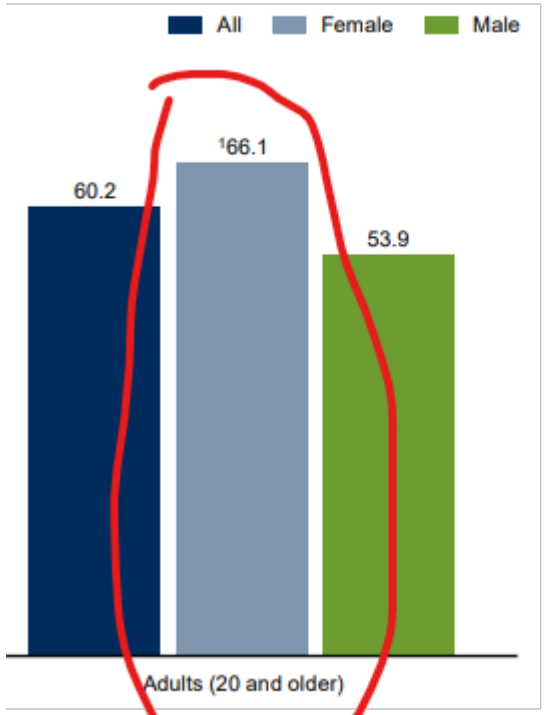
[1]Significant increasing linear trend ($p < 0.05$).
NOTE: Youth are ages 0–19 years and adults are age 20 and older.
SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2013–2014 through August 2021–August 2023.

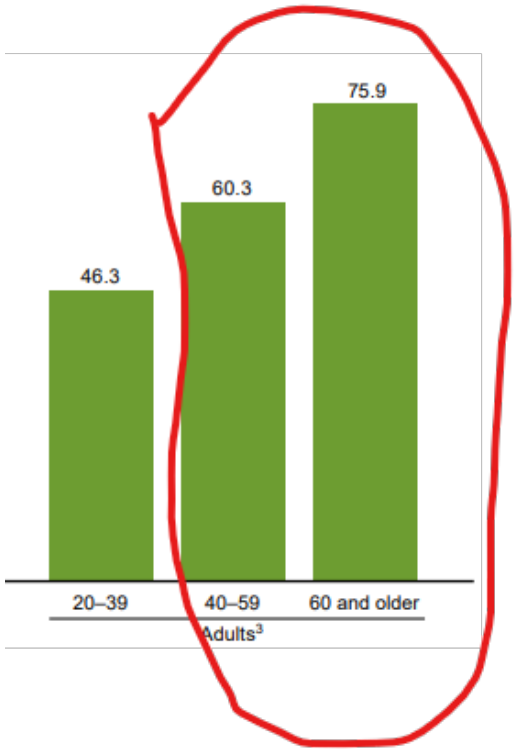
Stierman B et al. NCHS Data Brief. 2026: 561: 1-11

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Percentage use broken down by sex and age





Stierman B et al. NCHS Data Brief. 2026: 561: 1-11

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Four questions you should always ask when considering complementary medicine because the FDA is NOT asking them for you!

IS THERE EVIDENCE THAT IT WORKS FOR THE CONDITION FOR WHICH IT IS BEING PRESCRIBED?

IS IT SAFE IN THE DOSES PRESCRIBED FOR THE CONDITION IT IS BEING USED FOR?

ANSWER: THERE ARE NO HERBAL PRODUCTS FOR MENOPAUSE SYMPTOMS WHICH GET A RECOMMENDATION FROM THE MENOPAUSE SOCIETY

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Herbal products Questions 1&2

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Are they safe and effective?

Product	Level of evidence	Notes
Soy foods and extracts	Level II	Mixed evidence
Equol (soy metabolite)	Level II	Mixed evidence
Pollen extract	Level III	No by consensus and expert opinion
Amberen (ammonium succinate)	Level II	Limited manufacturer trials
Lactobacillus acidophilus	Level II	Very poor studies
Black Cohosh	Level I	Evidence doesn't work + hepatotoxicity
Wild Yam	Level II	Lack of data plus risk of harm
Dong quai	Level II	Evidence doesn't work + risk of harm
Evening primrose	Level II	Small study with no benefit shown
Maca	Level II	Study design problems
Ginseng	Level I	Evidence that it doesn't work
Labisia pumila	Level I	Evidence that it doesn't work
Chasteberry	Level II	Study design problems
Milk thistle	Level II	Limited very small study
Omega-3 fatty acid	Level I-II	Mixed, inconclusive data
Vitamin E	Level I	Very little evidence
Cannibinoids	Level II	Lack of evidence

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Questions 3 and 4!
Does the supplement you are buying actually contain the ingredients you are requesting? Or do they contain ingredients that you are not requesting?

FDA does not proactively regulate dietary supplements

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Quality of “Immune Support” dietary supplements sold online

Study

Case series of 30 “immune-health supplements” purchased from Amazon in 2021

Products analyzed using liquid chromatography – mass spectrometry and compared with labels

Key Findings

13/30 products had labels that accurately reflected content

13 products were “misbranded” because labeled ingredients were not detected

9 products had unlisted ingredients raising concerns about adulteration and safety

Crawford et al. *JAMA Network Open.* 2022;5(8):e2226040

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	 U.S. PHARMACOPEIA (USP)	 NSF INTERNATIONAL	 CONSUMERLAB.COM	
Contains ingredients listed on label	✓	✓	✓	✓
Does not contain contaminants	✓	✓	✓	✓
Dissolves within specified amount of time	✓	✓	✓	✓
Has been made according to Good Manufacturing Processes	✓	✓		✓

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Crawford et al. Analysis of select dietary supplement products marketed to support or boost the immune system. *JAMA Network Open.* 2022;5(8):e2226040

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CLINICAL CASE REVIEW

Cases to Consider Menopausal Hormone Therapy

Annie Gayman MD, Moderator
Sept 24, 2026



BEFORE YOU PRESCRIBE

Timing and hard stops

The window of opportunity

- Most favourable benefit–risk profile when started under age 60 or within 10 years of the final menstrual period.
- In that window, absolute risks of stroke, venous thromboembolism, and coronary events are low in healthy women.
- Starting later, or more than 10 years out, shifts the balance toward harm — particularly with oral estrogen.
- There is no arbitrary stopping date: reassess symptoms, risk, and preference at least yearly.

Contraindications to systemic therapy

- Unexplained vaginal bleeding — investigate first.
- Current, past, or suspected breast cancer; estrogen-dependent malignancy.
- Prior venous thromboembolism or pulmonary embolism, or known thrombophilia.
- Prior stroke, transient ischaemic attack, or myocardial infarction.
- Active liver disease with abnormal function.
- Pregnancy.

CASE 1

51-year-old, 14 months amenorrhoeic. Ten to twelve hot flashes daily and drenching night sweats waking her twice a night. BMI 24, blood pressure 118/74, no smoking. Uterus intact. No personal or family history of clot, stroke, or breast cancer.

CASE 1

51-year-old, 14 months amenorrhoeic. Ten to twelve hot flashes daily and drenching night sweats waking her twice a night. BMI 24, blood pressure 118/74, no smoking. Uterus intact. No personal or family history of clot, stroke, or breast cancer.

What to consider

- Squarely inside the age window — under 60
- Outside a year from her final period.
- Symptom burden is high and non-hormonal measures have not helped her sleep.
- No contraindications; baseline cardiovascular and breast risk are low.

Reasonable approach

Systemic estrogen with a progesterone for endometrial protection, since the uterus is intact. Start at the lowest effective dose, review at 3 months, and confirm mammography and blood pressure are up to date.

CASE 2

43-year-old, periods are generally regular but sometimes heavy and sometimes light. She has lower energy, gaining weight and experiences insomnia (not responsive to melatonin, trazodone). BMI 29, blood pressure 134/74, no smoking. Uterus intact. No personal or family history of clot, stroke, or breast cancer.

CASE 2

43-year-old, periods are generally regular but sometimes heavy and sometimes light. She has lower energy, gaining weight and experiences insomnia (not responsive to melatonin, trazodone). BMI 29, blood pressure 134/74, no smoking. Uterus intact. No personal or family history of clot, stroke, or breast cancer.

What to consider

- Symptom burden is less specific but destabilizing
- Periods have become irregular
- No contraindications; has possible HTN, breast risk are low.

Reasonable approach

Cannot say definitive impact of perimenopause. (Can occur 8-10 years before cessation of menses, lab evaluation not helpful).
Evaluate for mood disorders, alcohol use, stressors, sleep hygiene, diet.
Consider a lab evaluation with TSH, CBC.
Estrogen supplementation is not associated with weight loss at the population level and weight gain is not an indication for HRT.
If electing trial of MHT, consider contraception and desire for method to stop/decrease menses.

CASE 3

38-year-old with 14 months of amenorrhoea, elevated FSH on two occasions, and low estradiol. Mild flushes but her main concern is long-term health. Family history of osteoporosis. No contraindications.

CASE 3

38-year-old with 14 months of amenorrhoea, elevated FSH on two occasions, and low estradiol. Mild flushes but her main concern is long-term health. Family history of osteoporosis. No contraindications.

What tips the decision

- This is replacement of a physiological deficit, not symptom-driven treatment of an older woman.
- Untreated early estrogen loss raises risks of osteoporosis, cardiovascular disease, and cognitive decline.
- She needs higher doses than a woman in her fifties, and contraception if pregnancy is possible.

Reasonable approach

Offer hormone therapy until around the average age of natural menopause, about 51, then reassess as you would any other patient. A combined hormonal contraceptive is an alternative if contraception is also needed.
Typical dose 2mg estradiol PO daily or equivalent.
Lab monitoring recommended.

CASE 4

52-year-old with brain fog and occasional hot flashes. BMI 34, migraine with aura, and a maternal history of deep vein thrombosis. Has had 2 periods in the last year. Blood pressure well controlled on a single agent. Uterus intact.

CASE 4

52-year-old with brain fog and occasional hot flashes. BMI 34, migraine with aura, and a maternal history of deep vein thrombosis. Has had 2 periods in the last year. Blood pressure well controlled on a single agent. Uterus intact.

What tips the decision

- Oral estrogen carries first-pass hepatic effects and a higher venous thromboembolism risk.
- Transdermal estradiol has not been associated with the same excess clot risk in observational data.
- Migraine with aura is not a contraindication to transdermal therapy, though it does argue against oral combined contraceptives.

Reasonable approach

Transdermal estradiol as patch, paired with micronized progesterone for endometrial protection. Address weight, blood pressure, and lipids in parallel.

CASE 5

64-year-old, twelve years postmenopausal, requesting hormone therapy after a friend's recommendation. Moderate flushes persist. Hypertension and hyperlipidaemia, both treated. No prior vascular event.

CASE 5

64-year-old, twelve years postmenopausal, requesting hormone therapy after a friend's recommendation. Moderate flushes persist. Hypertension and hyperlipidaemia, both treated. No prior vascular event.

What tips the decision

- More than ten years out and over 60 — the absolute risks of stroke and clot are meaningfully higher.
- New initiation this far from menopause is generally discouraged for symptom control alone.
- Effective non-hormonal options exist and should be offered first.

Reasonable approach

Shared decision making between non-hormonal treatment options: a SSRI or SNRI, gabapentin at night, or a neurokinin-3 receptor antagonist where available.
If symptoms remain disabling, low-dose transdermal therapy is possible, but the higher risk must be explicit.

CASE 6

58-year-old, eight years postmenopausal. History of Right breast DCIS 10 years ago. No flushes. Reports vaginal dryness, painful intercourse, and two urinary tract infections this year.

CASE 6

58-year-old, eight years postmenopausal. History of Right breast DCIS 10 years ago. No flushes. Reports vaginal dryness, painful intercourse, and two urinary tract infections this year.

What tips the decision

- Isolated genitourinary symptoms do not require systemic exposure.
- Low-dose vaginal estrogen produces minimal systemic absorption and is generally continued long term (OK with breast cancer history per ACOG/Menopause Society)
- Symptoms are progressive without treatment — they will not resolve on their own.

Reasonable approach

Low-dose vaginal estrogen, with moisturizer and lubricant as adjuncts. Progesterone for endometrial protection is not routinely needed at low vaginal doses. Investigate any bleeding that occurs.
If systemic symptoms were present, use non-hormonal options
Any systemic MHT requires oncology consultation. Duavee is under investigation for this population. Duavee has equine estrogen with Bazedoxifene instead of progesterone. Bazedoxifene is a SERM that blocks estrogen effects in the uterus and breasts.

PUTTING IT INTO PRACTICE

Counselling and follow-up

- Frame risk in absolute terms, not relative. The excess breast cancer risk with combined therapy is small and dose- and duration-dependent; estrogen alone after hysterectomy carries little or no excess.
- Set expectations: flushes usually improve within four to eight weeks; genitourinary symptoms take longer and need continued treatment.
- Review at three months, then at least yearly — symptoms, side effects, blood pressure, and ongoing indication.
- Investigate any unscheduled bleeding after the first six months.
- Keep screening current: mammography and cervical screening
- There is no fixed duration. Stopping is a shared decision, and symptoms may return when therapy is withdrawn.



THE BOTTOM LINE

Individualise by symptom, timing, and risk — not by age alone.

Symptom first

Match the treatment to what actually bothers the patient — systemic for vasomotor symptoms, vaginal for genitourinary ones.

Timing matters

Under 60 and within ten years of menopause is where benefit most reliably outweighs risk.

Route matters

Transdermal estradiol is the safer default whenever thrombotic or metabolic risk is elevated.

GYN SEXUAL HEALTH:
Evidence-Based Approaches

Andrew Warner, MD, FACOG

OB/GYN Cap Hill

9/24/26

HUGE TOPIC

- Three main pearls

  HSDD (medications)

  How to find sex therapists

  Very quick introduction to other topics/resources

OVERVIEW

Female sexual dysfunction

- -HSDD
- -Female sexual arousal disorder
- -- Orgasm disorders

- -Appendix
- - Sexual history taking

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HSDD



Decreased Sexual Desire Screener (DSDS)

1. In the past, was your level of sexual desire/interest good and satisfying to you?	No □	Yes □
2. Has there been a decrease in your level of sexual desire/interest?	No □	Yes □
3. Are you bothered by your decreased level of sexual desire/interest?	No □	Yes □
4. Would you like your level of sexual desire/interest to increase?	No □	Yes □
5. Please check all the factors that you feel may be contributing to your current decrease in sexual desire/interest:		
A. An operation, depression, injuries, or other medical condition	No □	Yes □
B. Medications, drugs or alcohol you are currently taking	No □	Yes □
C. Pregnancy, recent childbirth, menopausal symptoms	No □	Yes □
D. Other sexual issues you may have (pain, decreased arousal, orgasm)	No □	Yes □
E. Your partner's sexual problems	No □	Yes □
F. Dissatisfaction with your relationship or partner	No □	Yes □
G. Stress or fatigue	No □	Yes □

Clinical assessment of patient answers is required.

- On average, the DSDS took < 15 minutes to complete in a clinical study (N = 921)
- DSDS had a sensitivity of 0.836 (84%) and a specificity of 0.878 (88%) (N = 263)

NO to Q1, 2, 3, or 4 = Not generalized acquired HSDD

YES to all Q1–4 and clinician-verified NO to all Q5 factors = Generalized acquired HSDD

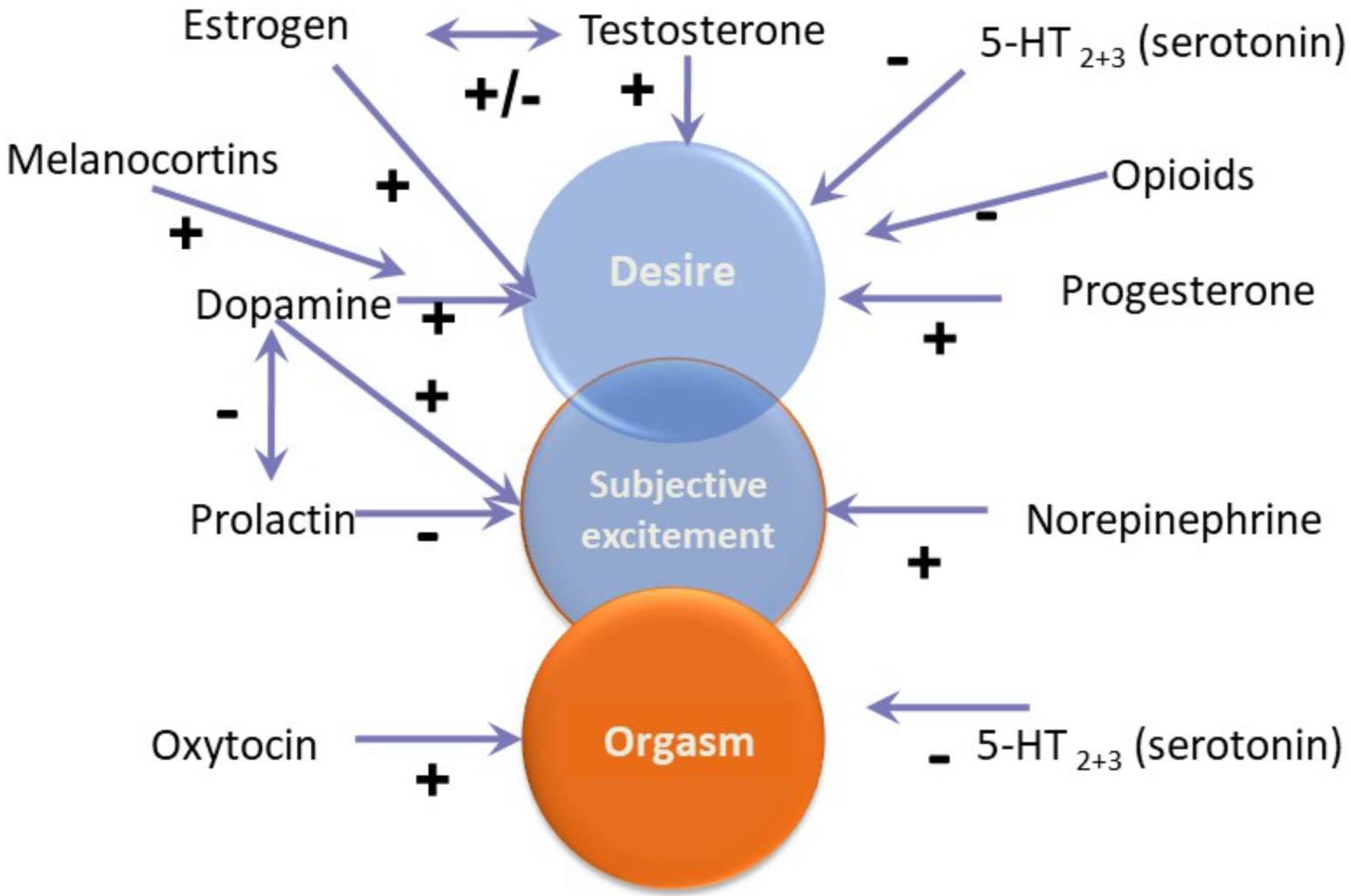
YES to all Q1–4 and YES to any Q5 factor = clinician to use best judgment to determine diagnosis

This figure was published in the Journal of Sexual Medicine, Vol 6. Clayton AH, Goldfischer ER, Goldstein I, et al. Validation of the decreased sexual desire screener (DSDS): a brief diagnostic instrument for generalized acquired female hypoactive sexual desire disorder (HSDD). Copyright Elsevier 2009.

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Central Effects of Neurotransmitters and Hormones on Sexual Functioning



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This figure was published in the Journal of Sexual Medicine, Vol 4. Clayton AH, Epidemiology and neurobiology of female sexual dysfunction. Copyright Elsevier 2007.

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Hypoactive Sexual Desire Disorder (HSDD)

Manifests as ***any*** of the following:

- Lack of **motivation** for sexual activity as manifested by either:
  - **Reduced or absent spontaneous desire (sexual thoughts or fantasies)**
  - **Reduced or absent responsive desire to erotic cues and stimulation or inability to maintain desire or interest through sexual activity**
- Loss of desire to **initiate or participate** in sexual activity, including behavioral responses such as avoidance of situations that could lead to sexual activity, that is not secondary to sexual pain disorders
- AND is combined with **clinically significant personal distress** that includes frustration, grief, incompetence, loss, sadness, sorrow, or worry.

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HSDD: Medical, Medication, and Substance Factors

Medical & Psychiatric Conditions

Depression
Urinary Incontinence
Neurological Disease
Cancer
Genitourinary Syndrome of **Menopause**
AIDS
Endocrine

- **Hypothyroidism/Hyperthyroidism**
- Hypothalamic amenorrhea
- Primary ovarian insufficiency
- Adrenal insufficiency
- Hypopituitarism
- Pituitary tumors
- Hyperprolactinemia
- Following oophorectomy
- Diabetes
- Obesity
- Metabolic Syndrome

Medications

Psychopharmacologic

- **Antidepressants**
- **Antipsychotics**
- Barbiturates
- Benzodiazepines
- Hypnotics

Hormones

- **Oral contraceptives**
- Gonadotropin releasing agonists and analogs
- Anti-androgens (eg, spironolactone)
- Anti-estrogens
- Other
- Cholesterol-lowering agents
- Beta-blockers
- Chemotherapeutics

Substances of Abuse

- Legal
- Controlled
- Illegal

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Physical Exam to Evaluate Factors Affecting Desire

TABLE 1. Physical Examination to Evaluate Other Factors Contributing to Decreased Desire

Condition	Assessment
Clitoral adhesions/phimosis or clitoral atrophy	Visual examination under magnification
Urethral meatal prolapse, telescoping of urethral meatus	Visual examination under magnification
Vulvodynia	Assess sensitivity to pressure with cotton swab around vestibule from 1-o'clock to 11-o'clock positions
High-tone pelvic floor dysfunction	Manual examination
Labial resorption; vulvar, vestibular, or vaginal atrophy	Visual examination under magnification, vaginal smear (wet mount)
Vulvar dystrophies and dermatoses	Visual examination under magnification, biopsy if needed
Pudendal nerve disorder	Assess tenderness at ischial spine, assess tenderness of pelvic floor muscles
Lumbar-sacral spinal pathology	Quantitative sensory testing, bulbocavernosus reflex latency testing, magnetic resonance imaging of lumbar and sacral spine

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Interventions

- Education including patient +/- partner
  - Provide information on normal sexual functioning and contributing/maintaining factors
  - Individualize care
    - Determine patient preferences for intervention(s)
    - Management principles that account for risk/benefit ratio, degree of invasiveness, cost
- Manage modifiable factors
- Medications
  - CNS active agents e.g. flibanserin, bremelanotide (premenopausal)
  - Postmenopausal women: Hormones e.g. testosterone, estrogen (local/systemic), DHEA (vaginal)
- Psychotherapy e.g. cognitive behavioral therapy (CBT), mindfulness-based CBT, sex therapy, couples therapy

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Flibanserin

- Mixed post-synaptic 5HT1A agonist and 5HT2A antagonist-exact mechanism unknown
  - 5HT1A agonists could have pro-sexual effects
  - 5HT2A antagonists could have pro-sexual effects
- Activity at dopamine D4 receptors and moderate affinity for 5HT2B and 5HT2C receptors
- Region-specific elevations in dopamine and norepinephrine offset inhibitory serotonergic activity resulting in increased desire pathways
- Serotonin may act as sexual satiety signal

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Flibanserin

- FDA-approved for **acquired, generalized HSDD** in **premenopausal** women not caused by:
  - Medical or psychiatric condition
  - Relationship problem
  - Effects of a medication/drug
- **100 mg PO daily at bedtime**
  - "Administration during waking hours increases risks of hypotension, syncope, accidental injury, and CNS depression" (10/2019 label)
  - Missed doses should be skipped
- May take up to 4 weeks for effects and 8-12 weeks for full response
  - If no response, discontinue at 8 weeks
  - *No data on duration of treatment, "neuroplasticity"

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Flibanserin & Alcohol Guidance

- Wait at least 2 hours after 1-2 standard alcoholic drinks before taking flibanserin at bedtime
- If consumed 3 or more standard drinks that evening, skip flibanserin dose at bedtime
- After taking flibanserin at bedtime, avoid alcohol until the following day
- Removed REMS requiring physicians to be certified & patients to sign form agreeing to abstain from alcohol

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Flibanserin – Contraindications & Warnings

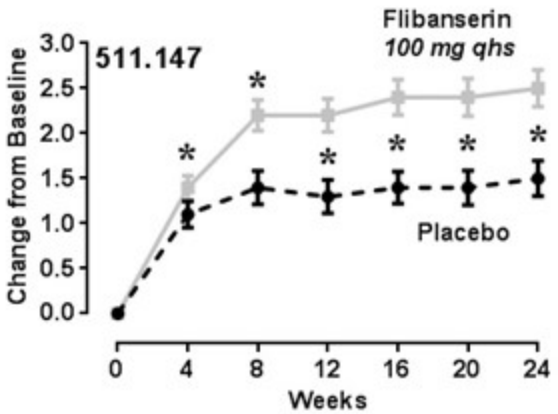
- Contraindications
  - Hepatic impairment
  - Concomitant use of moderate/strong CYP3A4 inhibitors
    - Wait 2 weeks after last dose of CYP3A4 inhibitor
    - Start CYP3A4 inhibitor 2 days after last dose of flibanserin
    - e.g. HIV drugs, antifungals (fluconazole), antibiotics (ciprofloxocin, macrolides), diltiazem
- Considerations
  - OCs (weak CYP3A4 inhibitors) may increase exposure to flibanserin & AEs
  - SSRI/SNRIs may slightly increase anxiety, somnolence, fatigue, insomnia, and dizziness
  - Dedicated SSRI/SNRI study did not increase rates of AEs or psychiatric symptoms
  - Concomitant use of other CNS depressants may increase risk of CNS depression

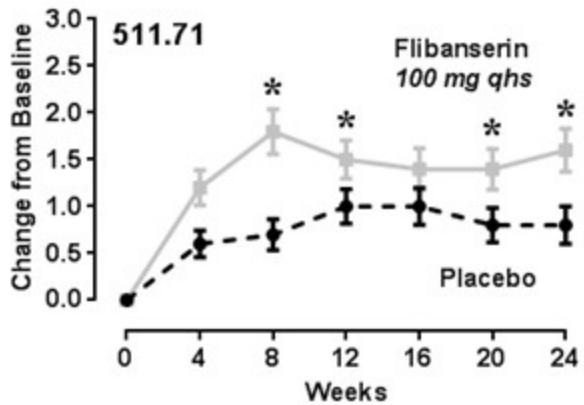
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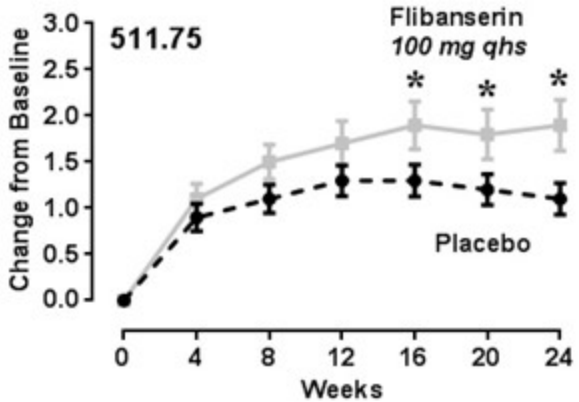
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Flibanserin Trials: Satisfying Sexual Events

Statistically significant separation from placebo in 4-8 weeks(*p < 0.05)







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Efficacy of Flibanserin

Efficacy of Flibanserin in Three Phase 3 Trials*		
Endpoint	Mean baseline	Improvement over baseline
Satisfying sexual events	2–3/mo	0.5–1.0/mo (median)
FSFI desire (range, 1.2–6.0)	1.8–1.9	0.3–0.4
Daily desire (range, 0–84)	10–12	1.7–2.3
Distress (range, 0–4)	3.2–3.4	0.3–0.4

*Improvement data represent least-square means, unless otherwise noted. The improvement in daily desire was not statistically significant. FSFI denotes Female

Sexual Function Index. For the FSFI and daily desire scales, the higher the number,

the greater the sexual desire. For the distress scale, the higher the number,

the greater the distress.

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From New England Journal of Medicine, Joffe HV, Chang C, Sewell C, et al., FDA approval of flibanserin--treating hypoactive sexual desire disorder, 374, 101-104. ©2016 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

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Common Adverse Events in ≥ 1% of Premenopausal Women

Preferred Term	Placebo n=1905 (%)	Flibanserin 100 mg qhs n=1542 (%)
Dizziness	41 (2.2)	176 (11.4)
Somnolence	59 (3.1)	173 (11.2)
Nausea	71 (3.7)	161 (10.4)
Fatigue	95 (5.0)	142 (9.2)
Insomnia	46 (2.4)	75 (4.9)
Dry mouth	17 (0.9)	37 (2.4)
Anxiety	17 (0.9)	28 (1.8)
Constipation	9 (0.5)	25 (1.6)
Abdominal pain	15 (0.8)	23 (1.5)
Sedation	3 (0.2)	20 (1.3)
Vertigo	6 (0.3)	16 (1.0)

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Bremelanotide Use

Indicated for the treatment of premenopausal women with acquired, generalized HSDD NOT due to:

- A co-existing medical or psychiatric condition
- Problems with the relationship, or
- Effects of a medication or drug/substance

- Inject 1.75 mg/0.3 ml solution subcutaneously via autoinjector to abdomen or thigh at least 45 minutes before anticipated sexual activity
- On demand, one-time use, injected in 5 seconds, fine-gauge nonvisible needle
- One dose per 24 hours to minimize effects of transient BP increase
- Maximum 8 per month
- Not indicated for HSDD in postmenopausal women or men
- Not indicated to enhance sexual performance
- Contraindication: uncontrolled hypertension or known cardiovascular disease

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Important Safety Information

CONTRAINDICATIONS

- VYLEESI is contraindicated in patients who have uncontrolled hypertension or known cardiovascular disease.

WARNINGS AND PRECAUTIONS

- **Transient increase in blood pressure and decrease in heart rate:** VYLEESI transiently increases blood pressure and reduces heart rate after each dose. Advise patients that these changes usually resolve within 12 hours. VYLEESI is not recommended in patients at high risk for cardiovascular disease. Consider the patient's cardiovascular risk before initiating VYLEESI and periodically during treatment and ensure blood pressure is well-controlled. To minimize the risk of more pronounced blood pressure effect patients should not take more than one VYLEESI dose within 24 hours. Patients should not use more than 8 VYLEESI doses per month.
- **Focal hyperpigmentation:** Reported by 1% of patients who received up to 8 doses per month, including involvement of the face, gingiva and breasts. Patients are at higher risk of developing focal hyperpigmentation if they have darker skin and with daily dosing. Resolution of the focal hyperpigmentation was not confirmed in all patients after discontinuation of VYLEESI. Consider discontinuing VYLEESI if hyperpigmentation develops.
- **Nausea:** Reported by 40% of patients who received up to 8 monthly doses, requiring anti-emetic therapy in 13% of patients and leading to premature discontinuation for 8% of patients. Nausea improves for most patients with the second dose. Consider discontinuing VYLEESI or initiating anti-emetic therapy for persistent or severe nausea.

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Adverse Events in >4% of Patients

Adverse Event, n (%)	Pooled Phase 3 Studies	
	Placebo (n=620)	VYLEESI (n=627)
Nausea	8 (1.3)	251 (40.0)
Flushing	2 (0.3)	127 (20.3)
Injection site reactions*	52 (8.4)	83 (13.2)
Headache	12 (1.9)	71 (11.3)
Vomiting	1 (0.2)	30 (4.8)

*Includes injection site pain, unspecified injection site reactions, erythema, hematoma, pruritus, hemorrhage, bruising, paresthesia, and hypoesthesia.

- The majority of adverse events were reported as mild (31%) to moderate (40%) and transient
- Discontinuation rates were 18% in the VYLEESI group vs 2% in the placebo group
- Discontinuation due to nausea was 8% in the VYLEESI group vs 0% in the placebo group
  - Median onset of nausea was within one hour and lasted about two hours in duration
  - Incidence of nausea was highest after first dose (reported in 21% of patients); declined to about 3% after subsequent doses

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MY SMART PHRASE:

"Addyi helps treats HSDD. It is used for premenopausal women. Take it at bedtime because it can cause tiredness. Wait two hours to take after using alcohol, skip dose if more than two drinks in a day. Side effects include dizziness, fatigue, and nausea. Stop using if not effective after 8-12 weeks if not affective. This medication leads to subtle changes, won't make you instantly have strong desire.

Bremelanotide - on demand injection. Take it at night (it has a 24 hour impact even though it says to take it two hours before sexual activity. Nausea is the main side effect, so the first time you use it use it alone. If you have nausea let me know so I can prescribe an anti-nausea medicine. You can't use it more than 8 times a month. If you have uncontrolled high blood pressure or cardiovascular disease you shouldn't use it."

FEMALE SEXUAL AROUSAL DISORDER



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FCAD & FGAD

Female Cognitive Arousal Disorder (FCAD)

- Characterized by the distressing difficulty or inability to attain or maintain adequate mental excitement associated with sexual activity as manifested by problems with feeling engaged and/or mentally turned on or sexually aroused, for a minimum of six months

Female Genital Arousal Disorder (FGAD)

- Characterized by the distressing difficulty or inability to attain or maintain adequate genital response including vulvovaginal lubrication, engorgement of the genitalia, and sensitivity of the genitalia associated with sexual activity, for a minimum of six months
- Disorders related to: Vascular and neurological injury or dysfunction

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Genital Arousal

- This can be more physiologic
  - Again consider medications
    - Systemic contraceptives
    - Antidepressants
  - Other comorbidities
    - Neurologic disorders
    - Diabetes
    - Trauma
    - Dermatitis



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LOCAL SEX THERAPISTS

I recommend trying this website (https://www.aasect.org/find-professional/2/WA/T%2BC) to find a sex therapist. If that doesn't work I am including some names and numbers of folks but this list is old and hasn't been updated in many years.

Here is a list of some local therapists:

Libby Livingston, NE Seattle 206-527-8774

Marilyn Germano, Factoria 425-241-2410

Michael Kelch, Edmonds 206-522-2808

Jill Seipel, Bellevue 425-455-6784

Tina Sellers, Seattle 206-281-2950

Beatrice Ellis, Seattle 206-324-7954

Louisa Terner, Wallingford 206-633-7951

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Types of Interventions

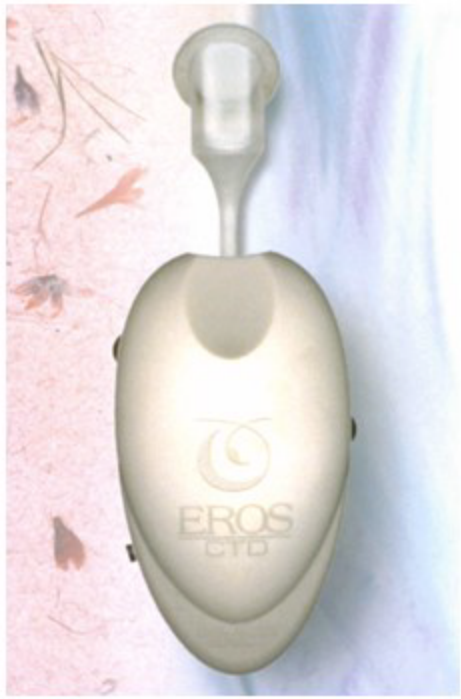
- Psychotherapy: Individual or Couples
- Physical therapy
- Pharmacologic therapies
- Adjunctive and alternative therapies

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FSAD: Non-Pharmacologic Genital Arousal Treatments

- Increasing stimulation
  - Vibrators, Pelvic Floor PT
- Eros Clitoral Therapy Device



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ORGASM DISORDERS/PERSISTENT GENITAL AROUSAL DISORDER

Characteristics of PGAD/GPD

Table 2. ISSWSH consensus expert opinion on criteria and characteristics of persistent genital arousal disorder/genito-pelvic dysesthesia (PGAD/GPD)

Criteria	persistent or recurrent, unwanted or intrusive, distressing sensations of genital arousal
	duration of ≥3 months
	may include other types of **genito-pelvic dysesthesia** (eg, buzzing, tingling, burning, twitching, itch, pain)
	most commonly experienced in the clitoris but also in other genito-pelvic regions (eg, mons pubis, vulva, vestibule, vagina, urethra, perineal region, bladder, and/or rectum)
	may include being on the verge of orgasm, experiencing uncontrollable orgasms, and/or having an excessive number of orgasms
	not associated with concomitant sexual interest, thoughts, or fantasies
Associations	limited resolution, no resolution, or aggravation of symptoms by sexual activity
	compromised orgasm quality (eg, aversive, impaired, altered frequency, intensity, timing, and/or pleasure)
	aggravation of genito-pelvic dysesthesia by certain circumstances (eg, sitting, car driving, music or sounds, general anxiety, stress, or nervousness)
	despair, emotional lability, catastrophization, and/or suicidality
	on physical examination, absent evidence of genital arousal (genital lubrication, swelling of clitoris or labia)

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Pharmacological Treatment

Table 5. Off-label pharmacological treatment strategies for symptom control of PGAD/GPD based on expert opinion. See package insert for dose ranges, adverse events, toxicity, drug interactions, contraindications, potential for abuse, and other safety information.

Category	References	Hypothesized Region of action	Commonly Prescribed medications	Potential Dosing Regimen
Anticonvulsants and non-opioid inhibitors of neurotransmission	122,139,155,156	S	carbamazepine gabapentin pregabalin topiramate lamotrigine oxcarbazepine	100 mg po, bid 100 mg po, tid; (maximum dose of 3,600 mg/d) 50 mg po, tid (maximum dose of 300 mg/d) 100 mg po, bid 50 mg po, qd; increase as needed 300 mg po, bid
Benzodiazepine GABA-ergic activators	157	S	clonazepam	0.25 mg bid
Non-benzodiazepine GABA-ergic activators	68	S	zolpidem	1 mg (compounded) tid or qid
Opioid Inhibitors of neurotransmission		4 - S	tramadol hydrocodone	50 mg po, bid or tid 5–10 mg po, qd (in combination with acetaminophen, 325 mg)
Tricyclic antidepressants	82	S	amitryptiline clomipramine desipramine nortriptyline	10 mg po qd (maximum dose of 150 mg/d) 25 mg po, qd (maximum dose of 250 mg/d) 100 mg po, qd (maximum dose of 300 mg/d) 25 mg po, tid (maximum dose of 150 mg/d)
SSRI/SNRI	156,158,159	S	duloxetine paroxetine	20 mg po, bid (maximum dose of 60 mg/d) 12.5 mg po, qd (maximum dose of 50 mg/d)
Dopamine antagonists or lowering agents	22,79,160,161	S	paliperidone risperidone varenicline	6 mg po, qd (maximum dose of 12 mg/d) 2 mg po, qd (maximum dose of 16 mg/d) 0.5 mg po, qd (maximum dose of 2 mg/d)
Specific Indications				
Hyperthyroidism		S N/A	methimazole propranolol	5 mg po, tid 40 mg po, bid (starting dose)
Restless leg syndrome				
Dopamine agonist	162	3–5	pramipexole	0.125 mg po, tid
Pelvic floor dysfunction		2		
Benzodiazepine			diazepam	2.5–10 mg, qd, vaginal/rectal suppository; in conjunction with physical therapy
GABA agonist	163,164		baclofen	20 mg, qd, vaginal/rectal suppository; in conjunction with physical therapy
Anti-cholinergic (neurotoxin)	165–167		botulinum toxin A	50–200 units, im, every 3 months

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Female Orgasmic Disorder

Diagnostic Criteria

- Presence of either of the following symptoms and experienced on almost all or all (approximately 75%-100%) occasions of sexual activity (in identified situational contexts or, if generalized, in all contexts):
  - Marked delay in, marked infrequency of, or absence of orgasm.
  - Markedly reduced intensity of orgasmic sensations.
- The symptoms have persisted for a minimum duration of approximately 6 months
- The symptoms cause clinically significant distress in the individual.
- The sexual dysfunction is not better explained by a nonsexual mental disorder or as a consequence of severe relationship distress (e.g., partner violence) or other significant stressors and
  is not attributable to the effects of substance/medication or another medical condition.
  - All specifiers apply (lifelong, acquired, generalized, situational, mild, moderate or severe)
  - Specify if:
    - Never experienced an orgasm under any situation

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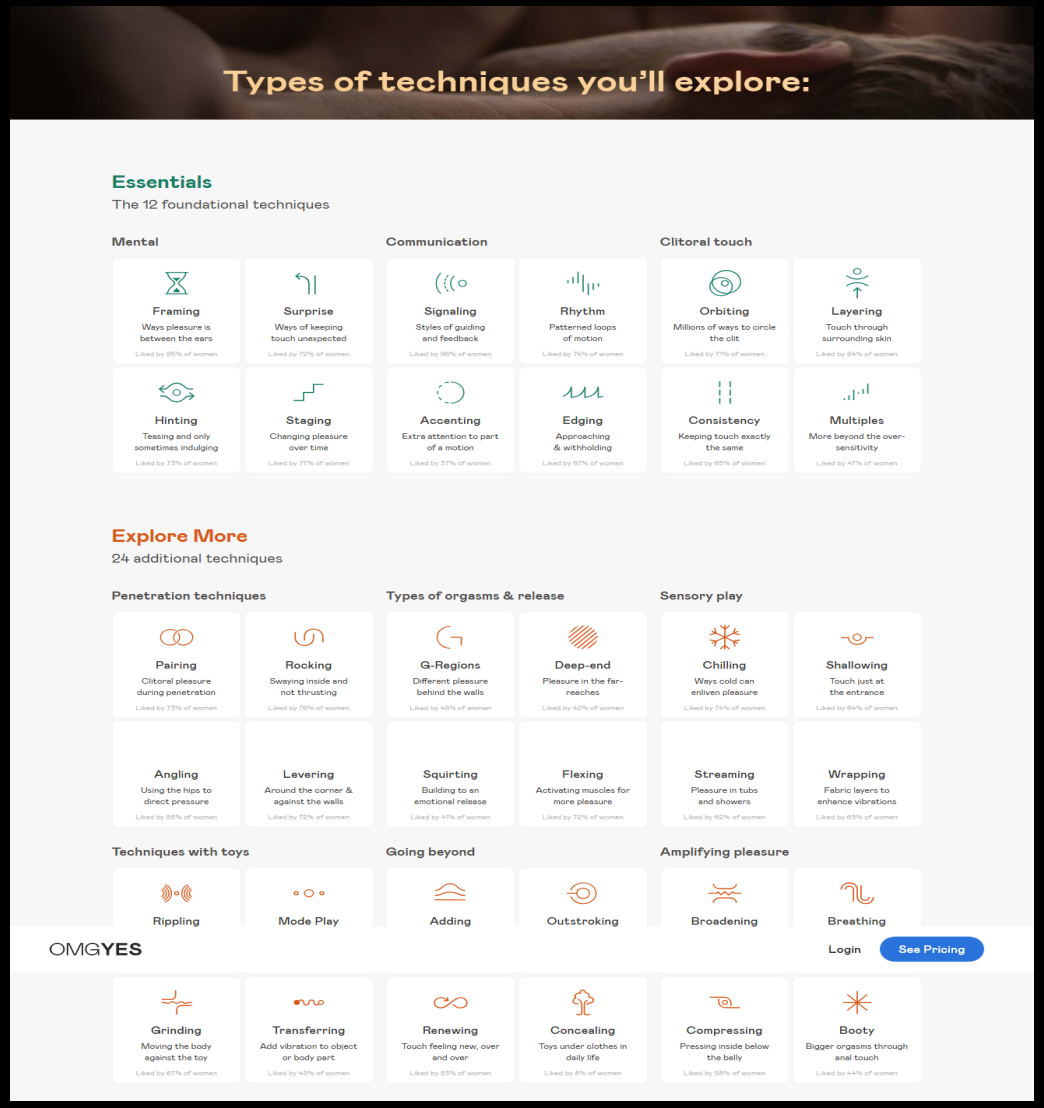
Female Orgasmic Disorder: Sex Therapy

- Cognitive Behavior Therapy (CBT) has been empirically shown to be effective
- Aim: Change attitudes and sexually relevant thoughts, decrease anxiety and increase orgasmic ability
- CBT techniques
  - Directed Masturbation
  - Sensate Focus
  - Systematic Desensitization
  - Sex Ed, communication skills training and Kegels too

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OMGYES



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North American Menopause Society 2014: Sexual Counseling

- Educate couples about normal, age-related sexual response changes in women (e.g., diminished lubrication, increased time for stimulation)
- Educate couples about normal, age-related sexual response changes in men (e.g., decreased rigidity, increased time for stimulation)
- Warm baths before genital activity
- Extended foreplay, lubricants

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North American Menopause Society: Sexual Counseling

- Sexual fantasies, erotica
- Experiment with non-coital activities: massage, oral stimulation
- Use masturbation as alternative to intercourse
- Change routine: location, time of day
- Change positions, other than “missionary”
  - “Coital alignment, women on top”

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Orgasmic Disorder: Treatment Options for Non-Therapists

- Permission by physician to:
  - Practice and explore self-stimulated/masturbation in privacy
  - Assert desired stimulation with partner
- Masturbation education
  - Described as common behavior and medical intervention
  - Describe types of masturbation
  - Distinguish and combine with dilators/incontinence devices
- Educate on vibrator use and types
- No FDA approved medical treatment for FOD
- No research on combined interventions

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TESTOSTERONE



Hormonal Levels in Healthy Premenopausal Women

Age Ranges	20 - 29 (n=17)	30 - 39 (n=23)	40 - 49 (n=20)
DHEAS ug/dL *Dehydroepiandrosterone Sulfate*	176.9 - 214.3	139.0 -170.8	124.7 - 156.1
SHBG nmol/L *Sex Hormone Binding Globulin*	43.6 - 58.6	44.6 - 52.4	47.0 - 58.4
Total T ng/dL *Total Testosterone*	45.5 - 57.5	27.6 - 39.8	27.0 - 38.6
FAI *Free Androgen Index*	3.72 - 4.96	2.04 - 2.96	1.98 - 2.94
Cal. Free T picomol/L *Calculated Free Testosterone*	21.5 - 27.2	13.4 - 19.5	12.4 - 17.8
ng/dL	0.6 - 0.8		

Reprinted with permission from Macmillan Publishers Ltd: International Journal of Impotence Research (Guay A, Munarriz R, Jacobson J et al. Serum androgen levels in healthy premenopausal women with and without sexual dysfunction: Part A. Serum androgen levels in women aged 20-49 years with no complaints of sexual dysfunction. Int J Impot Res 2004;16(2):112-120.), © 2004.

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Summary of Efficacy and Safety

- RCTs have established efficacy of transdermal patch for relieving symptoms of HSDD
  - Naturally and surgically menopausal women
  - With and without concomitant ET or EPT
- Main side effects: increased hair growth and acne
- Reassuring safety data, although inconclusive, with respect to cardiovascular, breast, endometrial outcomes
  - Long term safety data demonstrate no significant impact on intermediate metabolic endpoints and a low rate of cardiovascular events and breast cancer in post-menopausal women at increased cardiovascular risk.

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Global Statement: Summary and Key Messages

- International panel concluded only evidence-based indication for testosterone therapy for women is for **treatment of HSDD**.
- Data supports **moderate** therapeutic effect in **postmenopausal** women.
- Meta-analyses shows **no severe adverse** events during physiological testosterone use, with caveat that women at high cardiometabolic risk were excluded from study populations.
- **Safety of long-term** testosterone therapy has not been established.
- Diagnosis of HSDD involves full clinical assessment and that other factors contributing to FSD must be identified and addressed before testosterone therapy is initiated…guided by available diagnostic criteria (**ISSWSH** or **ICD 11).**
- A blood total testosterone level should not be used to diagnose HSDD (**NO CUTOFF**).

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Global Statement: Summary and Key Messages

- Treatment should only be with formulations that achieve blood concentrations of testosterone that approximate **premenopausal physiological concentrations**.
- As **no approved female product** is approved by a national regulatory body, **male formulations** can be judiciously used in female doses and blood testosterone concentrations must be monitored regularly.
- The panel recommended **against** use of **compounded testosterone**.
- The panel highlighted the pressing need for more research into testosterone therapy for women and the development and licensing of products indicated specifically for women.

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ISSWSH CPG for T Use: Key Messages

- Proper dosing should attain and maintain testosterone levels in the premenopausal physiological range.
- If an approved female formulation is not available, one-tenth of a standard male dose of 1% transdermal testosterone or about 300 mcg/day can usually achieve the normal premenopausal physiological range.
- Compounded testosterone, pellets, IM injections, and oral formulations are not recommended.
- Additional testing and alternative strategies may be required to assess failure to respond to typical testosterone treatment, particularly when testosterone or SHBG levels are high.

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Safety and Efficacy of Testosterone for Women

- 46 reports of 36 randomized controlled trials of **8,480 participants**
- Testosterone significantly increased sexual function, including **satisfactory sexual event frequency, desire**, arousal, orgasm, and self-image, and reduced distress in postmenopausal women.
- Associated with greater likelihood of reporting **acne** and **hair growth**
- No serious adverse events (**breast, intermediate CV endpoints**, uterus)
- Administration via non-oral routes (eg, **transdermal** application) preferred because of **neutral lipid profile**.

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Dosing Recommendations

- Men use 30 tubes or packets per month
- 1/10th – 1/15th of a tube or packet/day; 3 tubes/month
- Resealable tubes, room temp. (4 drops, syringe)
- Apply gel to skin surface, back of calf or thigh, upper outer thigh, or buttock (to avoid transference).
- Patients should be counseled that on average efficacy emerges 6 to 8 weeks after initiation of therapy.
- Many women feel improvement after 4 weeks, including reductions in distress, with maximal efficacy in 12 weeks.
- Generally not covered by commercial insurance
- Cost saving apps may be recommended:
  - GoodRx (www.goodrx.com)
  - SingleCare (www.singlecare.com)

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MONITORING AND FOLLOW-UP

- Baseline total testosterone should be measured before initiating therapy with repeat level in 3–6 weeks.
- Check T levels 6 weeks after dose increase and 2-3 weeks after supraphysiological level and dose decrease.
- Monitor for clinical response, assess for signs of androgen excess and decrease dose if side effects occur.
- Check serum total testosterone level every 4-6 months to screen for overuse and inherent androgenic consequences.
- If no benefit by 6 months, treatment should be ceased.
- If testosterone therapy results in improvement of HSDD, consider continuing for 6–12 months and then taking a drug holiday to see if further treatment is still required.
- In most cases, ongoing testosterone therapy is needed to maintain the improvement in HSDD.

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TESTOSTERONE

- No evidence that it helps postmenopausal women with bone density, lean body mass, muscle strength, cognitive function, general well being, mood or vasomotor symptoms.





- Global Consensus Position Statement on the Use of Testosterone Therapy for Women. The Journal of Clinical Endocrinology and Metabolism. 2019. Davis SR, Baber R, Panay N, et al.
- ACOG Practice Bulletin No. 141: Management of Menopausal Symptoms. Obstetrics and Gynecology. 2013

MY SMARTPHRASE: TESTOSTERONETHERAPY

Good to meet you today. We talked about your sexual health. We did a complete history and did not find any evidence of medicines, medical conditions, atrophy, vulvar or vaginal pain, or relationship issues that could be causing your concerns. We reviewed possible treatments such as hormone replacement therapy and mental health referral.

After this discussion we also reviewed considering treatment with testosterone. We discussed that this is considered off-label use and is NOT approved by the FDA for this use. You stated understanding of this and provided

consent to use testosterone despite it being used off label.

There is evidence that testosterone therapy in women will improve sexual function. There is data that transdermal testosterone doesn't increase the risks of breast and endometrial cancer. However, the data regarding ovarian cancer risk is inconclusive. Testosterone also doesn't appear to increase the risk of cardiovascular disease. None of this data has been studied long term.

Major side effects of testosterone therapy include hirsutism, acne, and decreased HDL cholesterol (for oral doses)

There are a number of preparations available but I recommend the following because it is easy to get in our system:

Testim tube. Apply a dime sized amount to a hairless region of your body nightly. 9 tubes (3 month supply) and 4 refills.

-If you could become pregnant, testosterone could be teratogenic (cause birth defects) so birth control is VERY important. You gave verbal consent that you understand this risk.

- If you are on anticoagulation therapy or insulin your levels will have to be monitored closely (insulin requirement can go down).

Please go to the lab 6 weeks after starting therapy so we can check your testosterone level.

You should notice a difference about 6-8 weeks after starting therapy. If you don't notice improvement by 6 months please stop using it.

If you do well on this medication consider stopping it after a year to see if you have lasting benefit even without the testosterone.

Dr. Andrew Warner, OB/GYN, 877-752-0423

MORE RESOURCES, GO KP!

OB/GYN Quick Care Guide | NATL Clinical Library

They test a lot! “Baseline monitoring of lipids, ALT/AST, and testosterone is required, then serial monitoring of serum testosterone levels at 1 month, 3 months, and 6 months, and then q6 months”

I don’t think liver enzymes need to be monitored at all. The endocrine society recommends testosterone at baseline, 6 weeks and every 6 months. I think every 6 months is excessive if patients are counseled on signs of hyperandrogenism.

- Recommended KPHC product: Testosterone (Androgel) 1% (50 mg/5 gram) TD Gel Pkt (product should be in 5g packet)
- Apply one-tenth of packet (a dime size amount equals 5mg) daily at bedtime to skin on back of calf. Store opened packet in a sealed container. Each packet contains 10 days of medication. (NOT to be applied to genitals)
- An exception code is needed since it is Non-Formulary
- Dispense Quantity: 90-day supply (9 packets of 5g each=45gm) with 0 refills
- Advise patients to wash hands after use
- Discontinue prescription if patient has no response after 3 – 6 months of use

Testosterone Clinical and Laboratory Monitoring

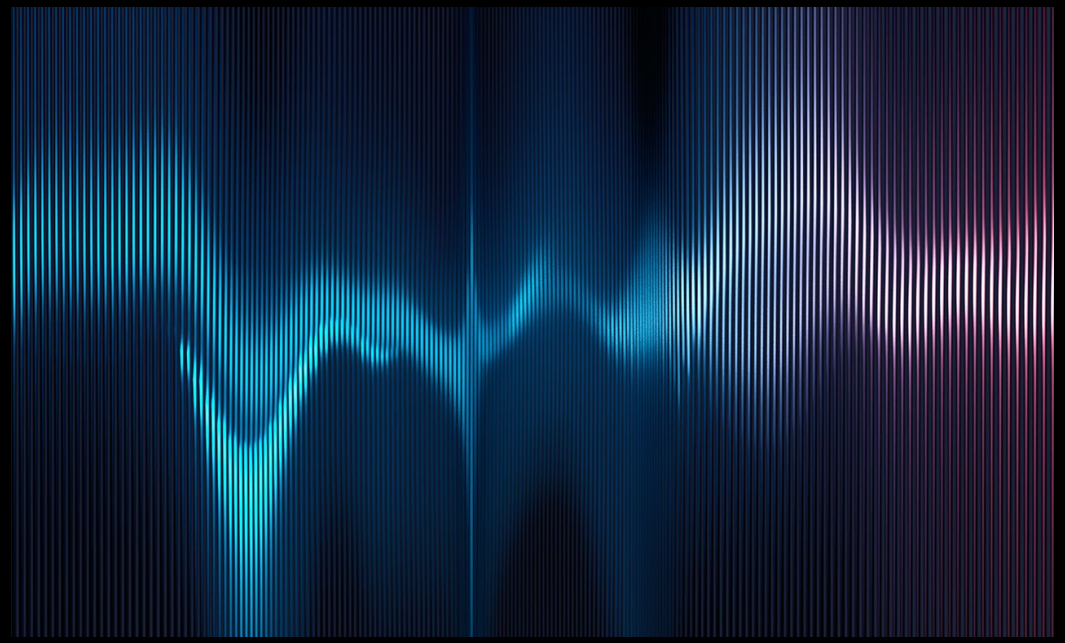
- Annual breast and pelvic exams
- Annual mammography
- Evaluation of abnormal bleeding
- Evaluation for acne, hirsutism, androgenic alopecia, voice changes, clitoromegaly
- Lipid profile, LFTs, CBC - baseline, 6 mos, annually
- Use for > 6 months contingent on clear improvement and absence of adverse events

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LUBE, MOISTURIZERS, VIBRATORS





Lubricants

Base	Ingredients	Safe with latex?	Staining	Comments
Water	Deionized water, glycerin, propylene glycol	Yes	No	Rarely causes irritation but dries out with extended activity
Petroleum	Mineral oil, petroleum jelly, baby oil	No; do not use with condoms, diaphragms, or cervical caps	Yes	Irritating to vagina
Natural oil	Avocado, olive, peanut, corn	Unclear (not recommended)	Yes	Safe (unless peanut allergy); non-irritating to vagina
Silicone	Silicone polymers	Yes	No	Non-irritating to vagina, long-lasting and waterproof

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Moisturizers

Product	Ingredients	Use	pH/Osmolality	Studies
Replens	Polycarbophil Glycerin, mineral oil	Every 3 days	3.0/2011	Yes
Luvena	Lactoperoxidase Lactoferrin	2x/wk		Yes
Hyalofemme	Hyaluronic acid	7 days > 2/wk	4.9/1729	HA-yes
Hyalo Gyn	Hyaluronic acid derivative Propylene glycol	2x/wk	4.8/1336	HA - yes
Sylk Natural Intimate	Extracts of kiwi fruit plant, vegetable glycerin, citric acid	2x/wk	4.47/877	No
Emerita Personal Moisturizer	Aloe vera gel, calendula, vitamin E, Ginseng, chamomile, allantoin	2x/wk		No
Yes Vaginal Moisturizer	Aloe barbadensis leaf juice, flax seed extract, citric acid	2x/wk	4.2/250	No

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DHEA for VVA/GSM

- DHEA 0.5% 6.5 mg vaginal suppository (Intrarosa) FDA-approved for treatment moderate to severe dyspareunia associated with VVA/GSM
  - Inserted intravaginally once daily at bedtime
  - Phase 3 trials reveal improvements compared to baseline over placebo of 4 coprimary objectives
    - Decreased percentage of parabasal cells
    - Decreased vaginal pH
    - Decreased pain with sexual activity
    - Improvement in moderate to severe vaginal dryness
  - Serum steroid levels remained well within normal postmenopausal range
  - Most common adverse effect: vaginal discharge due to melting vehicle (6%)
  - No change in endometrial atrophy after 12 months

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Prasterone- in the treatment for mild to moderate Urge Incontinence

Method- It was an observational prospective cohort study. Total 58 menopausal woman

Results- 58 woman, 29(50%) for treated with Prasterone and 29(50%) with hyaluronic acid suppositories. At the end of study, 26(89.7%) versus 3(10.3%) reported an improvement in the Prasterone versus hyaluronic acid group

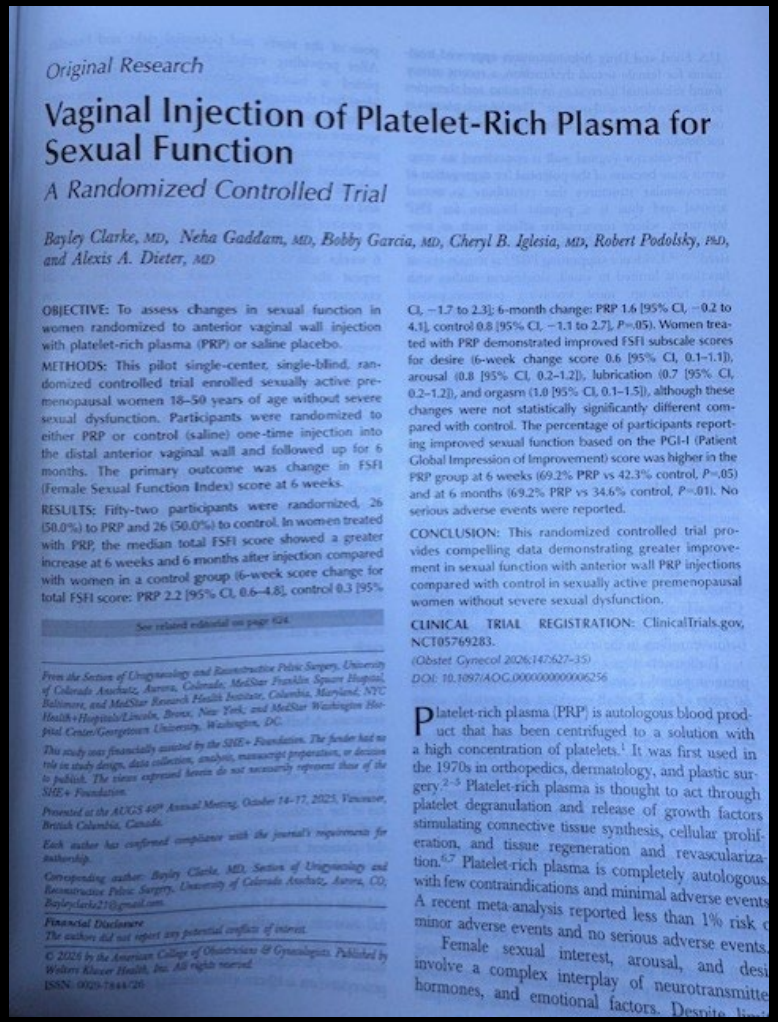
Conclusion- the study supported the hypothesis that Prasterone might improve severity of urinary urge incontinence in this set of woman.

As per the study, results need to be confirmed in further studies with the controlled desire and a large population

Menopause: The Journal of The North American Menopause Society

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THE FUTURE?



Original Research

Vaginal Injection of Platelet-Rich Plasma for Sexual Function

A Randomized Controlled Trial

Bayley Clarke, MD, Neha Gaddam, MD, Bobby Garcia, MD, Cheryl B. Iglesia, MD, Robert Podolsky, PhD, and Alexis A. Dieter, MD

OBJECTIVE: To assess changes in sexual function in women randomized to anterior vaginal wall injection with platelet-rich plasma (PRP) or saline placebo.

METHODS: This pilot single-center, single-blind, randomized controlled trial enrolled sexually active premenopausal women 18–50 years of age without severe sexual dysfunction. Participants were randomized to either PRP or control (saline) one-time injection into the distal anterior vaginal wall and followed up for 6 months. The primary outcome was change in FSFI (Female Sexual Function Index) score at 6 weeks.

RESULTS: Fifty-two participants were randomized, 26 (50.0%) to PRP and 26 (50.0%) to control. In women treated with PRP, the median total FSFI score showed a greater increase at 6 weeks and 6 months after injection compared with women in a control group (6-week score change for total FSFI score: PRP 2.2 [95% CI, 0.6–4.8], control 0.3 [95% CI, −1.7 to 2.3]; 6-month change: PRP 1.6 [95% CI, −0.2 to 4.1], control 0.8 [95% CI, −1.1 to 2.7], $P=.05$). Women treated with PRP demonstrated improved FSFI subscale scores for desire (6-week change score 0.6 [95% CI, 0.1–1.1]), arousal (0.8 [95% CI, 0.2–1.2]), lubrication (0.7 [95% CI, 0.2–1.2]), and orgasm (1.0 [95% CI, 0.1–1.5]), although these changes were not statistically significantly different compared with control. The percentage of participants reporting improved sexual function based on the PGI-I (Patient Global Impression of Improvement) score was higher in the PRP group at 6 weeks (69.2% PRP vs 42.3% control, $P=.05$) and at 6 months (69.2% PRP vs 34.6% control, $P=.01$). No serious adverse events were reported.

CONCLUSION: This randomized controlled trial provides compelling data demonstrating greater improvement in sexual function with anterior wall PRP injections compared with control in sexually active premenopausal women without severe sexual dysfunction.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, NCT05769283.

(Obstet Gynecol 2026;147:627–35)
DOI: 10.1097/AOG.0000000000006256

See related editorial on page 624.

Platelet-rich plasma (PRP) is autologous blood product that has been centrifuged to a solution with a high concentration of platelets.[1] It was first used in the 1970s in orthopedics, dermatology, and plastic surgery.[2–5] Platelet-rich plasma is thought to act through platelet degranulation and release of growth factors stimulating connective tissue synthesis, cellular proliferation, and tissue regeneration and revascularization.[6,7] Platelet-rich plasma is completely autologous with few contraindications and minimal adverse events. A recent meta-analysis reported less than 1% risk of minor adverse events and no serious adverse events.

Female sexual interest, arousal, and desire involve a complex interplay of neurotransmitters, hormones, and emotional factors. Despite [illegible]

From the Section of Urogynecology and Reconstructive Pelvic Surgery, University of Colorado Anschutz, Aurora, Colorado; MedStar Franklin Square Hospital, MedStar Research Health Institute, Columbia, Maryland; NYC Baltimore, and MedStar Research Health Institute, Columbia, Maryland; NYC Health+Hospitals/Lincoln, Bronx, New York; and MedStar Washington Hospital Center/Georgetown University, Washington, DC.

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Presented at the AUGS 45th Annual Meeting, October 14–17, 2025, Vancouver, British Columbia, Canada.

Each author has confirmed compliance with the journal's requirements for authorship.

Corresponding author: Bayley Clarke, MD, Section of Urogynecology and Reconstructive Pelvic Surgery, University of Colorado Anschutz, Aurora, CO; Bayleyclarke21@gmail.com.

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ADDITIONAL RESOURCES

- OMGYES.com
- ISSWSH - Home

APPENDIX

Principles for Sexual History Taking

- Patients prefer that health care provider initiate topic and advise (90%)
- Use simple, direct language; avoid euphemisms
- Private setting, patient clothed and comfortable
- Compassion, honesty, normalizing statements
- Declare and demonstrate lack of embarrassment
- Be aware of patient's cultural background
- Ensure confidentiality
- Avoid judgement and assumptions

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How to Conduct the Interview

- Use words and body language that put the patient at ease
  - Open, non-defensive body pressure
  - Sit and maintain eye contact
  - Avoid nervous gestures
  - Practice using sexual terminology
- Demonstrate comfort with conversation about sexual health
- Ask open-ended questions
  - Use silences to allow the patient to speak

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Language/Communication

- State an understanding or ask to learn about how cultural beliefs inform sexuality
- Effective use of interpretation services
  - Gender match between interpreter, patient, and provider
  - In-person vs. telephonic interpretation
  - Non-reliance on family interpreters
- Positive nonverbal communication
- Assure confidentiality
- Demonstrate comfort with conversation about sexual health

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“ALLOW” Algorithm

Managing sexual dysfunction in the office setting:

- A: Ask
- L: Legitimize
- L: Limitations ➡ Refer
- O: Open up for further discussion and evaluation
- W: Work together to develop a treatment plan

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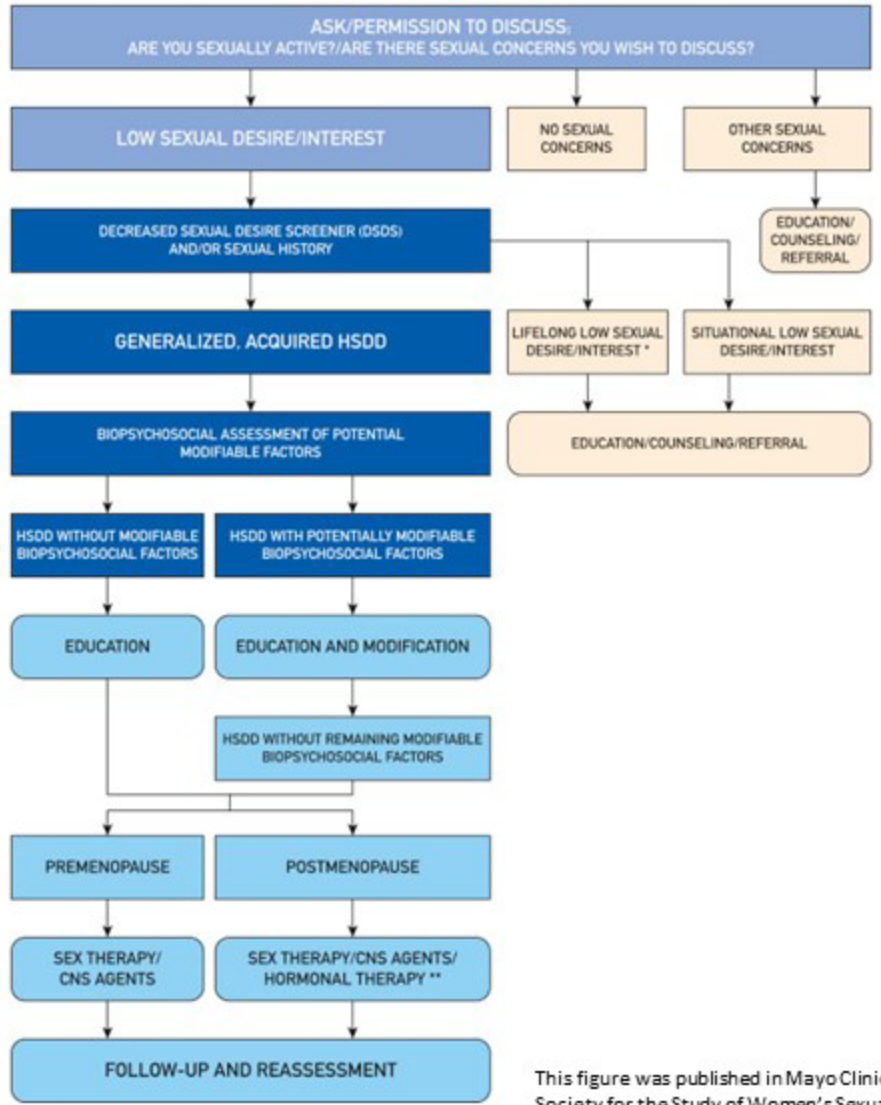
Office-Based Counseling: PLISSIT Model

- **P**: Permission to talk about sexual issues, reassurance, empathy
- **LI**: Limited Information
  - e.g., education about genital anatomy or educational resources
- **SS**: Specific Suggestions
  - e.g., use of lubricants, altering position
- **IT**: Intensive Therapy
  - e.g., referral for psychotherapy, sex/couples therapy

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ISSWSH Process of Care for Management of Hypoactive Sexual Desire Disorder (HSDD) in Women



This figure was published in Mayo Clinic Proceedings, Vol 93, Issue 4. Clayton AH et al. The International Society for the Study of Women's Sexual Health Process of Care for Management of Hypoactive Sexual Desire Disorder in Women. Copyright Elsevier 2018.

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Genitourinary Syndrome of Menopause

Recognition, treatment, maintenance, and risk-sensitive counseling

Jessica Yearwood MD FACEP MSCP

WPMG Menopause/Perimenopause for Primary Care
Continuing Medical Education
September 24, 2026



Learning objectives

Recognize

From patient symptoms to clinical diagnosis. Common presentations and differential consideration.

Compare

Local estrogen, DHEA, ospemifene, and nonhormonal options.

Maintain

Patient counseling and maintenance strategies for long term symptom management.

Counsel

Shared decision making in patients with oncology history, specifically breast cancer.

Clinical destination: symptom-matched, evidence-based treatment

Case: “I keep getting UTIs”

58-year-old patient

Urgency and nocturia
Burning with negative cultures
Three treated “UTIs” this year
New dyspareunia and reduced lubrication
Avoids discussing symptoms unless asked

Audience prompt

What would you ask next or like to know more about?

What findings would change the differential?

Would treatment require a moisturizer trial first?

GSM is a symptom-and-sign spectrum.



Vulvar / vaginal

Dryness
Burning
Irritation
Itching
Discharge
Exam pain
Tissue friability

Sexual

Reduced lubrication
Dyspareunia
Bleeding

Urinary

Urgency
Frequency
Dysuria
Nocturia
Recurrent UTI

VMS improve over time, but GSM generally worsens with prolonged estradiol deficiency beyond menopause. GSM is unlikely to improve without treatment. 100% will have changes occur. 40-50% bothered by symptoms.

Diagnosis: listen first, examine with purpose

Symptoms establish the syndrome. Examination supports the diagnosis and looks for alternatives.

Focused history

Location and quality
Urinary pattern and cultures
Sexual or exam pain
Bleeding, discharge, irritants
Cancer and treatment history

You may need to initiate the conversation and ask questions.

Targeted exam

Vulvar dermatoses
Tissue pallor and/or friability
Loss of rugae and/or elasticity
Introital narrowing and location of urethral meatus
Pelvic floor tenderness
Signs of prolapse

Test selectively

Urinalysis/culture if indicated
Vaginitis testing when appropriate
Biopsy or referral for lesions
Do not use hormones to confirm GSM

Differential Dx: Do not let “GSM” hide another diagnosis

Infection

UTI, candidiasis, BV, STI
Foreign body

Dermatosis

Lichen sclerosus/planus/simplex; dermatitis

Pain disorder

Pelvic floor hypertonicity; vulvodynia

Anatomic

Prolapse; urethral lesion; stenosis; trauma; treatment sequalae (surgery, radiation therapy)

Neoplasia

Persistent lesion, bleeding, or mass

Medication/systemic

Irritants; autoimmune or dermatologic disease
Other physiologic low estrogen states

Treatment Toolbox

Vaginal Estrogen	Restores vaginal blood flow, decreases vaginal pH, improves the thickness and elasticity of vulvovaginal tissue
Lubricants	Intended for use during sexual activity Reduce friction Increase lubrication and comfort
Moisturizers	Adhere to the vaginal mucosa, allowing cells to maintain moisture
Other options	Vaginal DHEA (dehydroepiandrosterone) Oral ospemifene Laser therapy (controversial)

Vaginal estradiol: multiple delivery options, same goal

Cream

Flexible dosing; useful when vulvar application is needed



Tablet or insert

Fixed dose, low mess, simple routine



Ring

Long interval between changes; steady local delivery



Match formulation to dexterity, comfort, cost, adherence, and symptom location.

Recurrent UTI: prevention with clinical and economic value

2024 model: estimated net savings of $1,226–$4,888 per treated patient per year



Clinical premise

Topical estradiol data were modeled as reducing infections from 5 a year to 0.5–2 a year.
This is a 42% relative risk reduction.

Systemic estradiol does not demonstrate same UTI reduction benefit.

Cost inputs

- $1,222 calculated cost per UTI
- Average therapy spending of $1,013 in 2020.
- Calculated $3-5K less UTI related spending per Medicare beneficiary per year.
- Net savings of $1-4K per year

Economic estimates are model-based and depend on assumptions, prices, and population.

Beyond estradiol: DHEA and ospemifene

Vaginal DHEA (prasterone)

Local intravaginal therapy

Guideline-supported option for dryness and dyspareunia

Metabolites: DHEA sulfate, testosterone, estradiol, estrone



Oral ospemifene

Systemic oral SERM (estrogen agonist/ antagonist)

Option for dryness and dyspareunia

Although ospemifene appears to have antiestrogenic effects on the breast, it is not approved for use with history of breast cancer

Similar to other SERM's, favorable effect on bone



A chronic condition needs a maintenance plan

Initiate

Align therapy with symptoms and preferred route. Explain correct use and goals.

Reassess

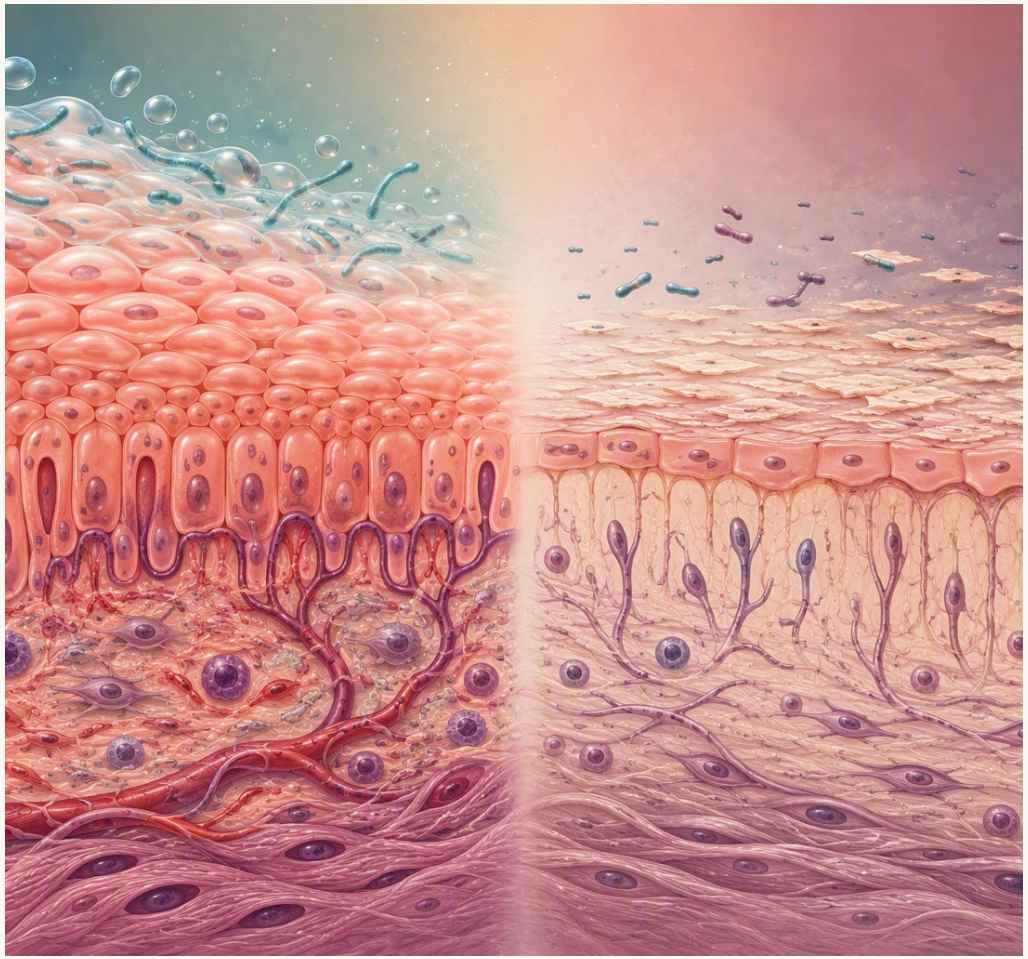
Review adherence, technique, adverse effects, response, and the differential.

Maintain

Continue the lowest-burden effective regimen; revisit if symptoms or goals change.

Set the expectation: ongoing treatment is needed to sustain benefit.

Breast cancer history: separate fear from evidence





Start with nonhormonal options

ACOG recommends nonhormonal methods as first-line care in this population.

If symptoms persist

Low-dose vaginal estrogen may be considered after discussion of risks and benefits, including for patients using Tamoxifen

If taking an aromatase inhibitor

Use shared decision-making among the patient, gynecologist, and oncologist.

Unlike tamoxifen, AIs do not block the effects of exogenous estrogens on breast tissue. With the concomitant use of both estrogen and an AI, there is the potential for elevated serum estrogen levels to stimulate estrogen receptors in breast tissue. However, when serum estradiol levels were evaluated in 10 studies, most demonstrated either only a transient increase (resolving within 12 weeks) or no increase at all in serum estrogen levels

Treatment of Urogenital Symptoms in Individuals With a History of Estrogen-dependent Breast Cancer. *Obstetrics & Gynecology.* 2021; 138 (6): 950-960. doi: 10.1097/AOG.0000000000004601.

What does the breast cancer safety evidence show?

2025 meta-analysis: no observed increase in recurrence, breast cancer mortality, or overall mortality



Evidence Based Findings

8 observational studies
24,060 patients in recurrence analysis
No randomized safety trial

The use of vaginal estrogen in patients with a history of breast cancer:

- Not associated with an increased risk of breast cancer recurrence (6 articles, 24,060 patients, OR 0.48; 95% CI 0.23–0.98).
- No increase in the risk of breast cancer mortality (4 articles, 61,695 patients, OR 0.60; 95% confidence interval 0.18–1.95).
- No increase in overall mortality (5 articles 59,724, OR 0.46; 95% CI 0.42–0.49).

Additional Guideline and Studies

- AUA GSM Guideline 2025 (endorsed by TMS and ISSWSH): local vaginal estrogen may be offered after breast cancer using shared clinical decision making.
- JAMA Oncology 2024: n 49,000 No increased breast cancer-specific mortality (HR 0.77)
- Danish registry study (JNCI 2022): no association with recurrence overall
- BMJ Medicine 2024: vaginal estradiol NOT associated with developing breast cancer

1. American Urological Association. Genitourinary Syndrome of Menopause: AUA/SUFU/AUGS Guideline. 2025.

2. Glynne S et al. Menopausal hormone therapy for breast cancer patients: what is the current evidence? *Menopause*. 2026;33(1):88–117. doi:10.1097/GME.0000000000002627.

3. Agrawal P, Singh SM, Able C, et al. Safety of Vaginal Estrogen Therapy for Genitourinary Syndrome of Menopause in Women With a History of Breast Cancer. *Obstet Gynecol.* 2023;142:660.

4. McVicker L, Labeit AM, Coupland CAC, et al. Vaginal Estrogen Therapy Use and Survival in Females With Breast Cancer. *JAMA Oncol.* 2024;10:103.

5. Meaidi A, Pourhadi N, Lokkegaard EC, et al. Association of vaginal oestradiol and the rate of breast cancer in Denmark: registry-based, case-control study nested in a nationwide cohort. *BMJ Med.* 2024;3:e000753.

6. Beste ME, Kaunitz AM, McKinney JA, Sanchez-Ramos L. Vaginal estrogen use in breast cancer survivors: a systematic review and meta-analysis of recurrence and mortality risks. *Am J Obstet Gynecol.* 2025;232(3):262–270.e1. doi:10.1016/j.ajog.2024.10.054.

An informed conversation that patients can hear

“Your symptoms fit GSM, a common tissue change related to lower estrogen. The symptoms often persist without ongoing treatment, but we have several effective options. We can choose a nonhormonal product, a local prescription treatment, or a combination based on what bothers you most. If you have had breast cancer, we will review your cancer therapy, what you have already tried, and the evidence together. For some patients, low-dose vaginal estrogen remains a reasonable option through shared decision-making.”

Five take-home points

1. Ask proactively: dryness is only one presentation.
2. Diagnosis is clinical; examination supports and excludes mimics.
3. **Local estrogen is a first-line prescription option, not a reward after moisturizer failure.**
4. For recurrent UTI plus GSM, recommend local low-dose vaginal estrogen when appropriate.
5. After breast cancer, use individualized, multidisciplinary shared decision-making.

Selected bibliography

GUIDELINES & CONSENSUS

ACOG Clinical Consensus No. 2. Treatment of Urogenital Symptoms in Individuals With a History of Estrogen-dependent Breast Cancer. 2021.

ACOG Committee Opinion No. 659. 2016. Replaced by the 2021 Clinical Consensus.

American Urological Association. Genitourinary Syndrome of Menopause: AUA/SUFU/AUGS Guideline. 2025.

North American Menopause Society. GSM Position Statement. Menopause. 2020;27(9):976–992.

SUPPORTING LITERATURE

Agrawal P, Singh SM, Able C, et al. Safety of Vaginal Estrogen Therapy for Genitourinary Syndrome of Menopause in Women With a History of Breast Cancer. Obstet Gynecol. 2023;142:660.

Beste ME, et al. Vaginal estrogen use in breast cancer survivors: systematic review and meta-analysis. AJOG. 2025;232:262–270.e1. PMID 39521301.

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Houston CG, et al. Cost Savings Analysis of Topical Estrogen Therapy in UTI Prevention. Urol Pract. 2024;11:257–266. PMID 38154005.

Kingsberg SA, Wysocki S, Magnus L, et al. Vulvar and vaginal atrophy in postmenopausal women: findings from the REVIVE survey. J Sex Med. 2013.

Mac Bride MB, Rhodes DJ, Shuster LT. Vulvovaginal atrophy. Mayo Clin Proc. 2010.

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Meaidi A, Pourhadi N, Lokkegaard EC, et al. Association of vaginal oestradiol and the rate of breast cancer in Denmark: registry-based, case-control study nested in a nationwide cohort. BMJ Med. 2024;3:e000753.

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Portman DJ, Gass MLS. Menopause. 2014;21(10):1063–1068.

Rahn DD, Carberry C, Sanses TV, et al. Vaginal estrogen for genitourinary syndrome of menopause: systematic review. Female Pelvic Med Reconstr Surg. 2014.

Suckling J, Lethaby A, Kennedy R. Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database Syst Rev. 2006.



MENOPAUSE AND CVD

Rachael Wyman, MD

Capitol Hill Cardiology

KEY TAKEAWAYS

- When evaluating a woman's risk for CVD incorporate reproductive risk into your shared decision-making conversation around prevention therapies
- Menopause is a cardiovascular inflection point
- Estrogen decline worsens vascular and lipid risk
- Hormone therapy is not recommended for prevention of cardiovascular disease
- Timing determines whether HT helps or harms from a cardiovascular perspective
- Shared decision making is key to treating cardiovascular risk as well as determining if and when HT should be used in any given patient

CASE

- 44 y.o. female with diabetes for 8 years, nonsmoker, hx of hysterectomy at age 20 due to uterine rupture during second pregnancy, presents for preventative care visit
- Exam: BMI 35 BP 120/75
- Labs
  - Total Cholesterol 244 HDL 41 TG 222
  - LDL 159 Non HDL Cholesterol 203
  - Ac 5.8

POLL

- What is the next best step?
  - Calculate risk using prevent risk score
  - Evaluate for risk enhancers
  - Start a statin
  - Check FSH levels to determine if this patient is in menopause

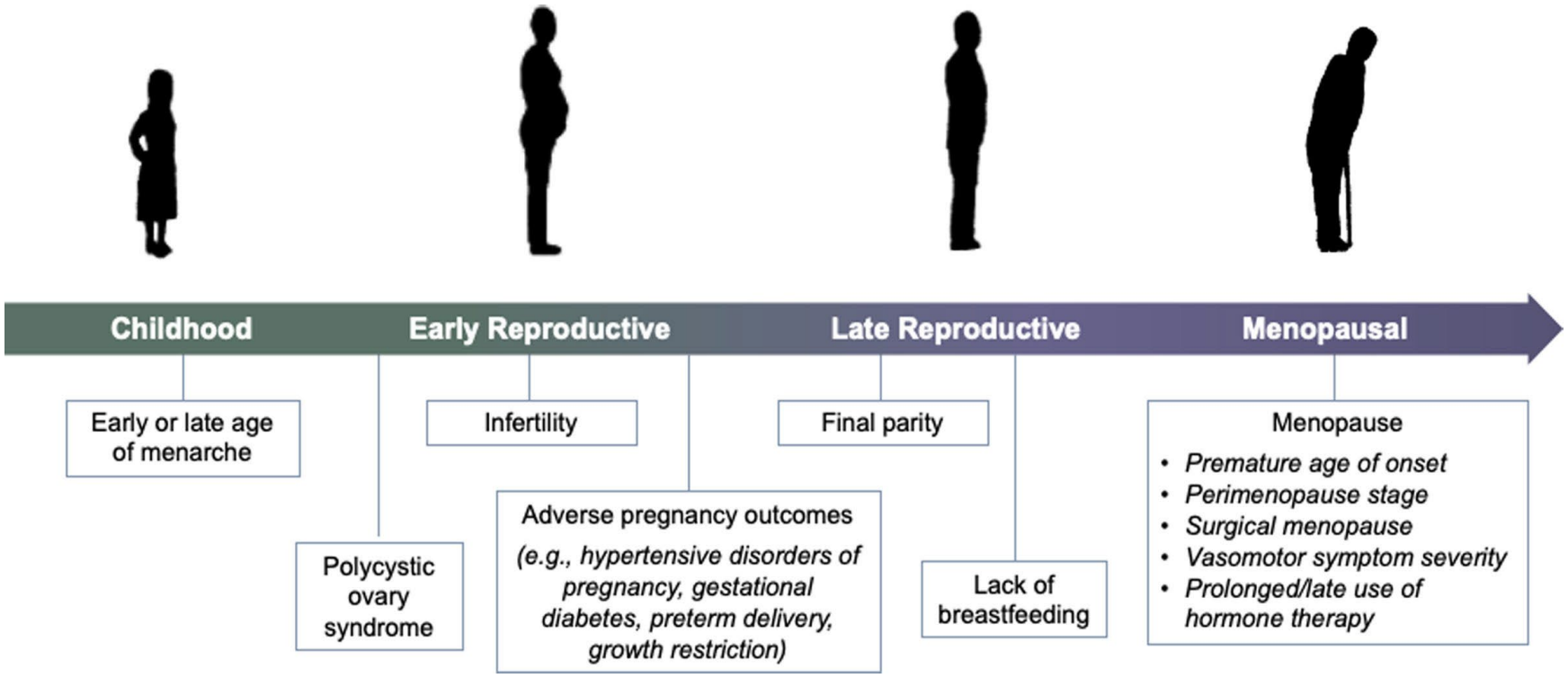
ASSESSING RISK

- PREVENT SCORE
  - 10 year risk 4.4%
    - Borderline Risk consider LLT
  - 30 year risk 25.4%
    - ≥10% a moderate intensity statin is reasonable
- In persons >40 years of age who have diabetes, CKD, or HIV statin therapy has demonstrated benefits even among those at lower absolute ASCVD Risk

ASSESSING RISK

- Risk Enhancers
  - Lpa
  - Hx of premature ASCVD in first degree relative
  - Higher risk ancestry (S. Asian, Filipino)
  - High polygenic risk
  - Chronic inflammatory disease
  - Hscrp
  - TG persistently ≥175
  - LDL persistently ≥160, non HDL ≥190
  - Reproductive risk markers
    - Menarche <10 years of age, PCOS, premature menopause <40 years of age, preeclampsia, gestational diabetes, gestational hypertension, premature delivery (before 37 week gestation), recurrent spontaneous pregnancy loss

Cardiovascular Risk Enhancers during a Woman's lifespan



Anna C. O'Kelly. Circulation Research. Pregnancy and Reproductive Risk Factors for Cardiovascular Disease in Women, Volume: 130, Issue: 4, Pages: 652-672, DOI: (10.1161/CIRCRESAHA.121.319895)

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PATIENT RECHECK

- Patient presents with symptoms of chest pressure radiating to the neck on the left side, started after covid infection, also has irregular heart beats, sometimes has vomiting with these spells, starts when being active, now on a low carb diet
- Medications included insulin, metformin, sertraline, lisinopril, glimepiride

POLL

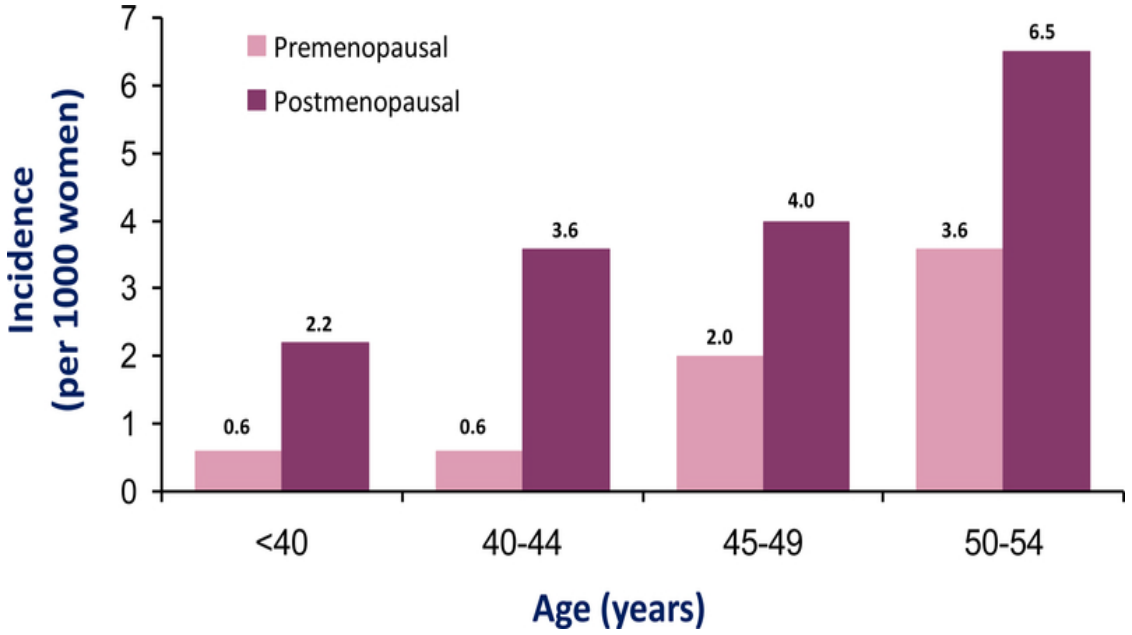
- What would you do next?
  - Order a Holter monitor
  - Order a stress test
  - Rx a PPI sounds like reflux
  - Order a TSH
  - Recommend increasing carbs in diet

PATIENT FOLLOW UP

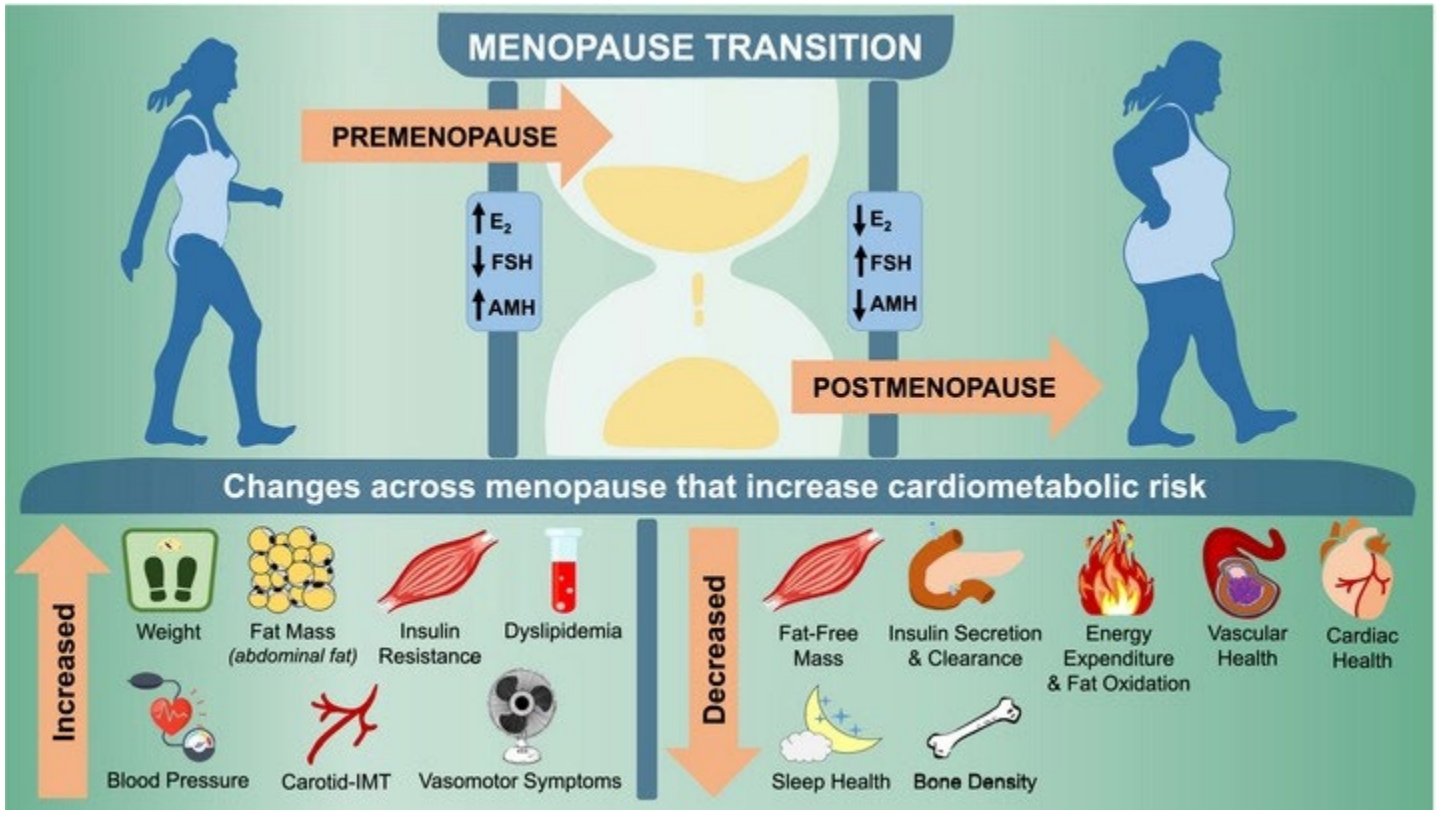
- Holter monitor was done with low burden of PVC's and TSH was normal
- No further work up or treatment was pursued
- 9 months later pt presented to ER with chest pain, had elevated troponin, coronary angiography showed multivessel coronary artery disease and she went on to have a CABG

CVD INCREASES POST MENOPAUSE

- Women have a lower incidence of CVD before menopause compared to men
  - Felt due to protective effects of estrogen
- An increase in CAD is typically seen about 10 years post menopause
  - Not necessarily due to estrogen loss but due to
    - Dyslipidemia
    - Insulin resistance
    - Fat redistribution
    - High blood pressure



Lerner D.J. Am. Heart J. 1986;111(2):383–390.
Kannel WB Ann Intern Med 1976;85:447–452



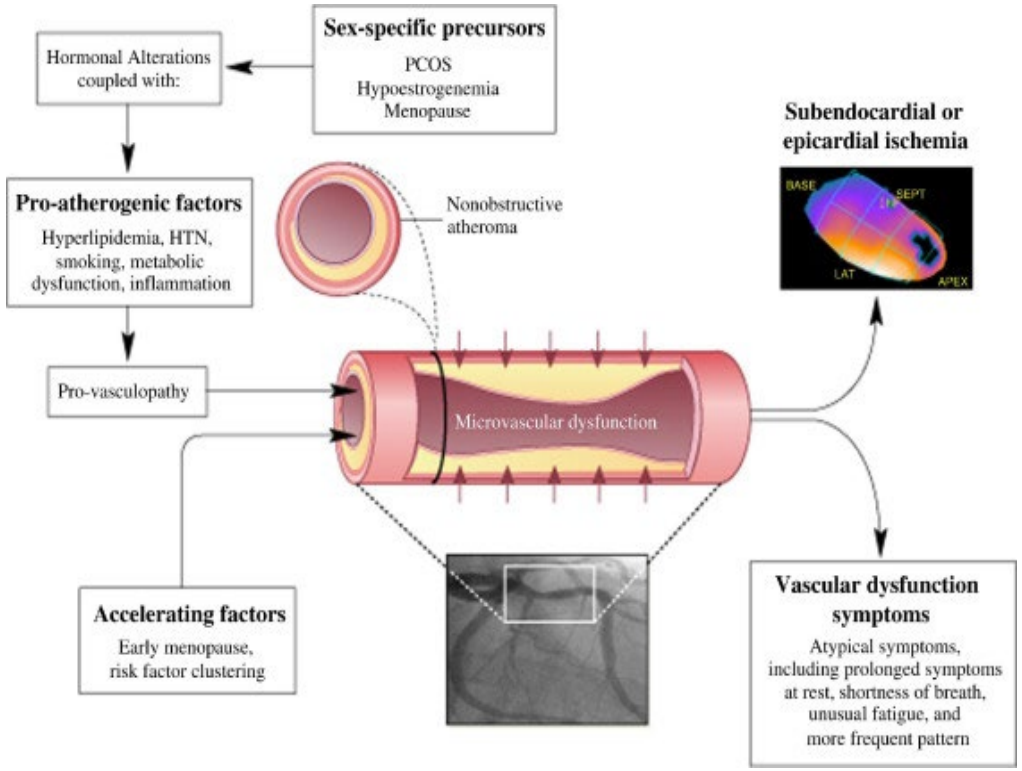
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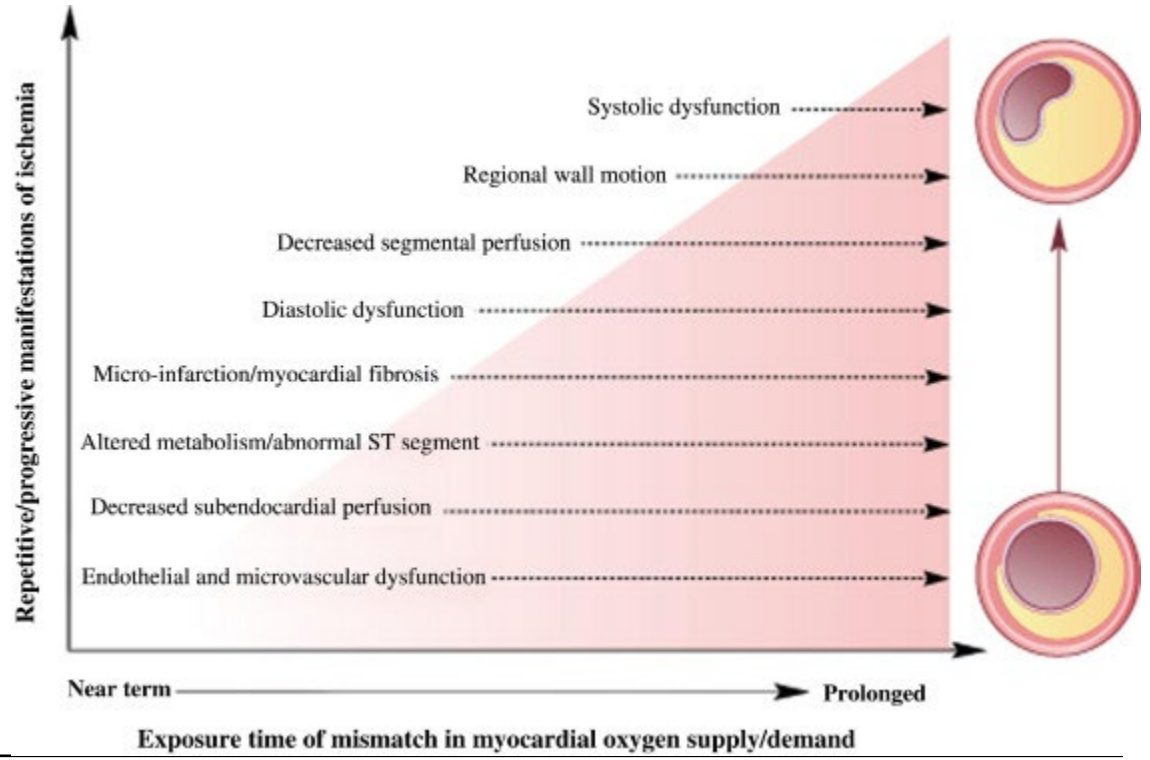
ESTROGEN AND ENDOTHELIAL FUNCTION

- Estrogen ↑ nitric oxide synthesis → vascular smooth muscle relaxation
- Estrogen ↓ the synthesis of Endothelin-1 a vasoconstrictor
- One trial of conjugated equine estrogen and transdermal estradiol vs placebo showed:
  - **Transdermal E decreased arterial stiffness and cell adhesion molecules and MCP-1, which are instrumental in recruitment of monocytes to arteries to promote atherosclerosis**
  - CEE increased CRP, no change arterial stiffness.
  - No change in control group.
  - Neither estrogen had effect on blood pressure
- Severity of hot flashes correlated with endothelial dysfunction

Sumino H, Ichikawa. Atherosclerosis. 2006 Dec;189(2):436-42

WHY ENDOTHELIAL FUNCTION MATTERS

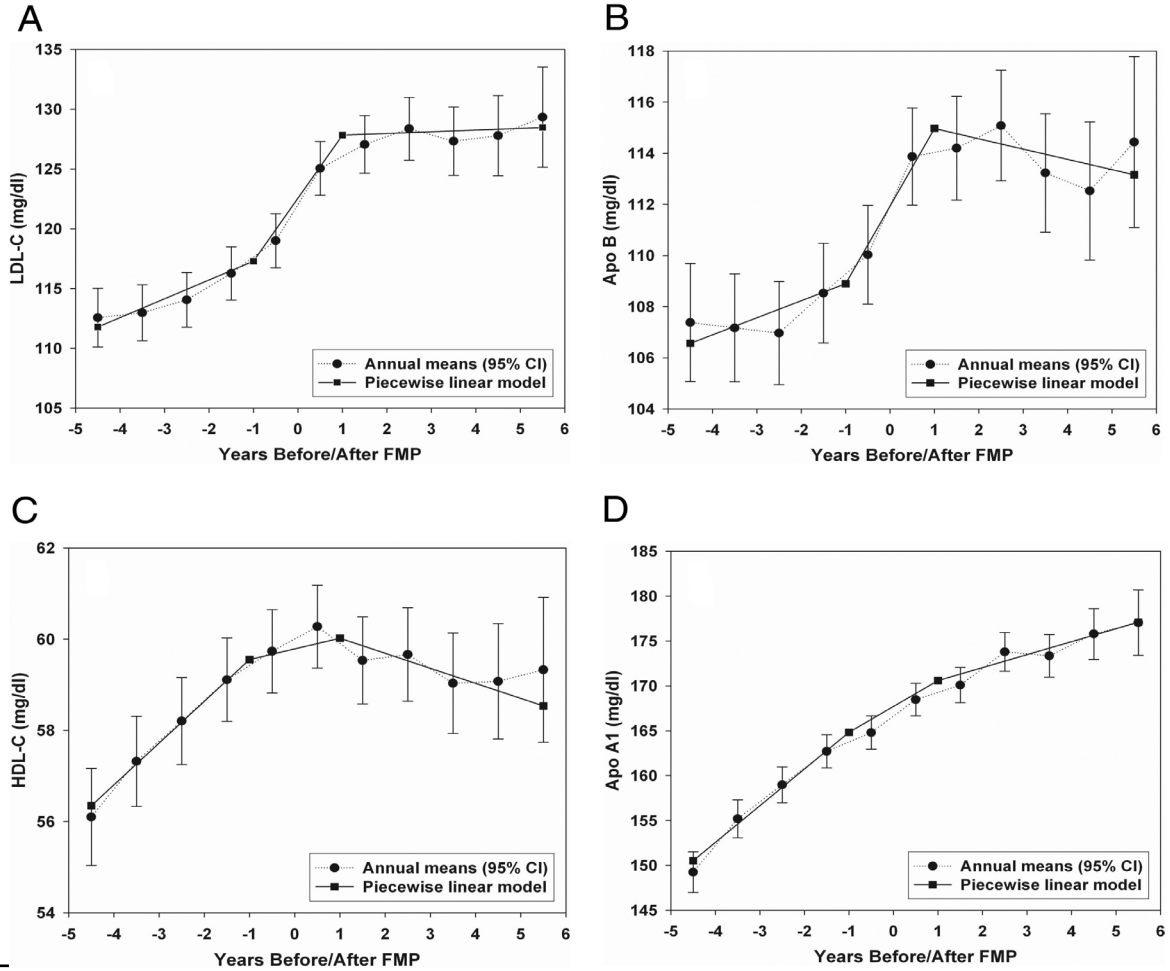




Shaw L, et al. JACC 54(17): 1561-1575

LIPID AND FAT CHANGES-THE SWAN STUDY

- TC, LDL and apoB all significantly increase in the 1-year interval around the final menstrual period-independent of the age at which it occurs
- No influence on blood pressure, insulin, glucose, Lpa
- Epicardial and paracardial adipose tissue increased in peri and post MP vs pre MP (9.9% and 20.7%)
- MRI assessments of body composition premenopausal vs ≈8 years postmenopausal, statistically significant increases in total abdominal fat, subcutaneous adipose tissue, and visceral adipose tissue but no significant changes in weight, waist circumference, or lean mass after adjustment for age



Matthews KA, J Am Coll Cardiol. 2009 Dec 15;54(25):2366-73.
Franklin RM, Metabolism. 2009 March 58(3): 311-315

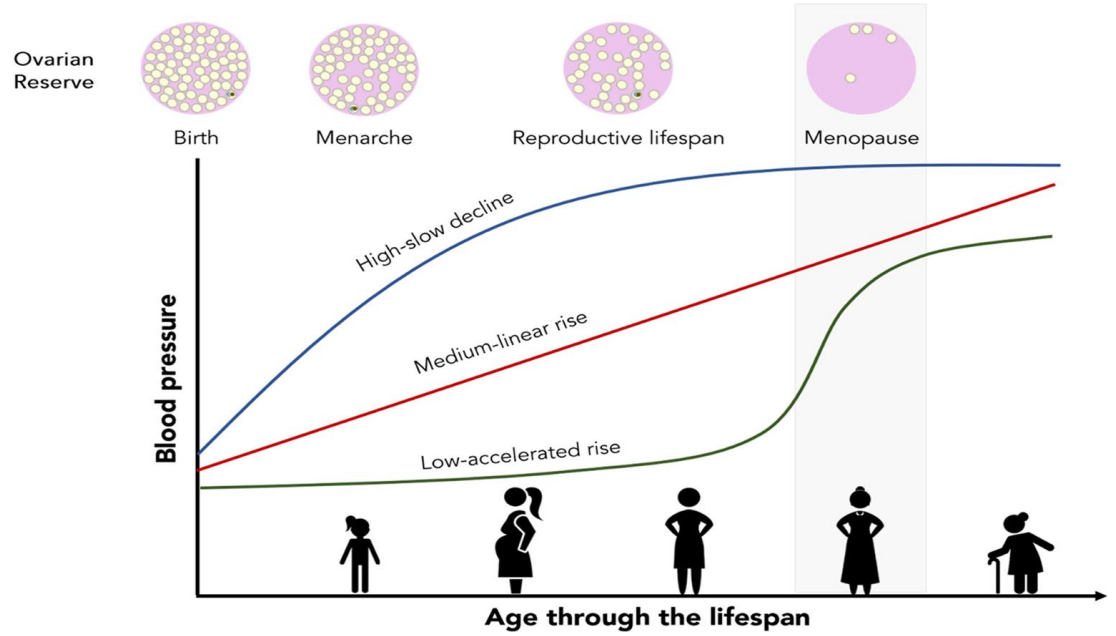
METABOLIC HEALTH AND MENOPAUSE

- Estradiol promotes peripheral fat distribution and improves insulin sensitivity
- Studies linking menopausal status and abdominal adiposity with insulin resistance and diabetes is mixed
- Increased abdominal adiposity and increased BMI are strongly linked to insulin resistance and associated with an increased risk for type 2 diabetes and cvd
- Risk of developing type 2 diabetes was significantly reduced in women who used HT in WHI and HERS

Marlatt KL, Pitynski-Miller DR, Gavin KM, et al. Body composition and cardiometabolic health across the menopause transition. *Obesity (Silver Spring)*. 2022; 30: 14–27

BLOOD PRESSURE TRAJECTORY THROUGH TIME

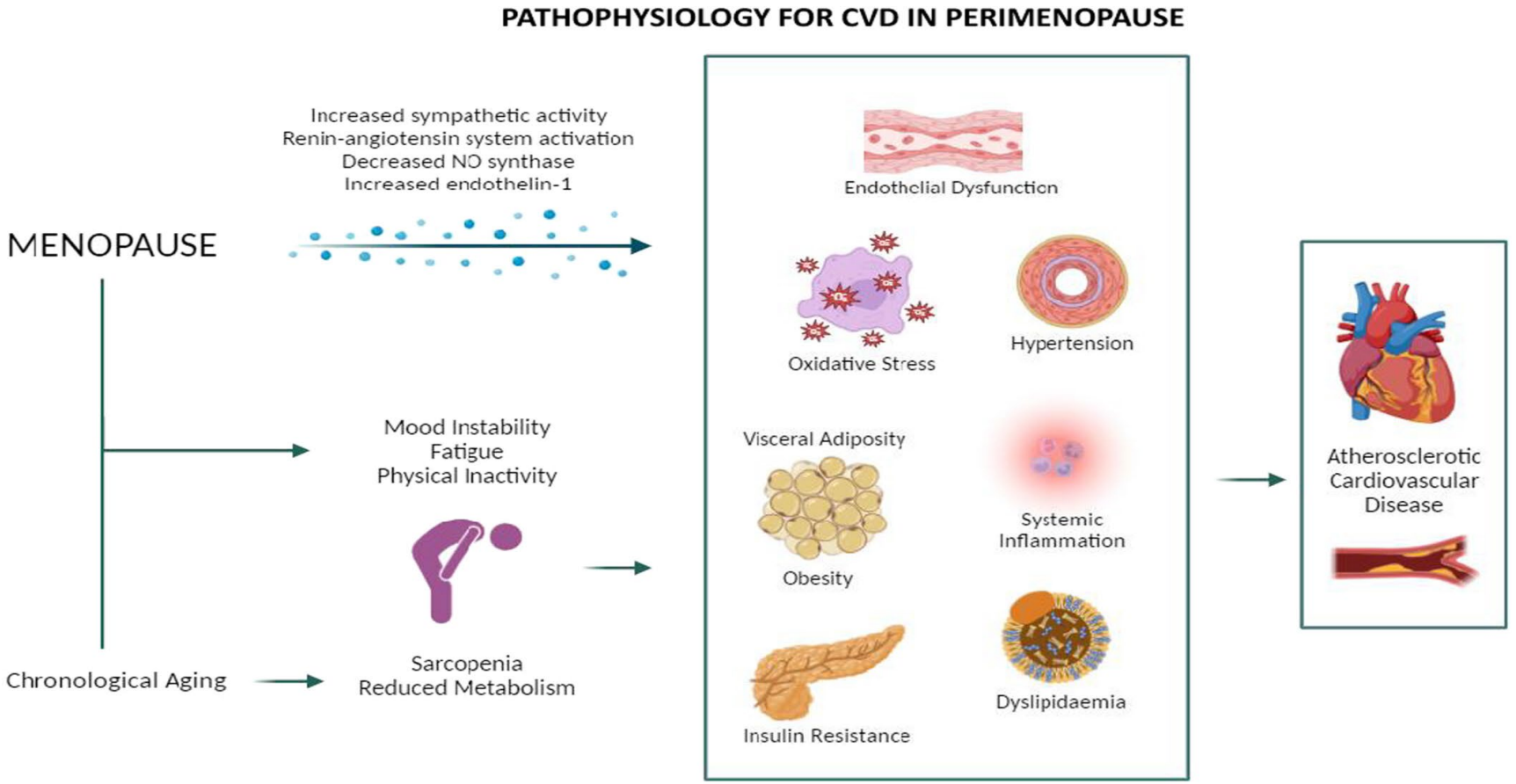
- 3 Trajectories identified
  - Low-accelerated rise felt due to Menopause transition
  - Linear trajectory consistent with chronologic aging
- Low-accelerated rise more likely to be seen in women with menopause before 51



MENOPAUSE AND BLOOD PRESSURE

- After controlling for chronologic aging, association between menopause transition and bp were inconclusive and inconsistent
- Using SWAN data there are distinct trajectory groups based on pattern and level of blood pressure over time in relationship to Final Menstrual Period
- The accelerated rise pattern within 1 year of the FMP suggests a menopause contribution
- Vasomotor symptoms predicted higher SBP, MAP, and pulse pressure
- Clinical pearl: ask about hot flashes when you see a newly elevated BP in a peri-menopausal woman

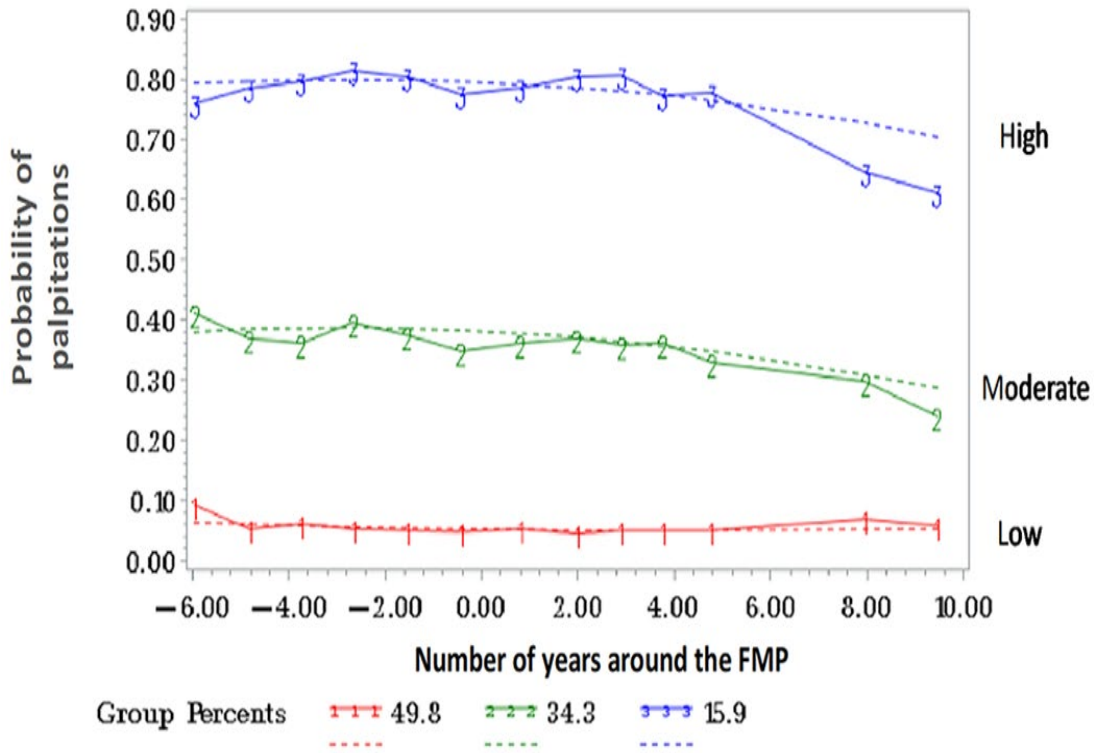
Samargandy S Trajectories of Blood Pressure in Midlife Women: Does Menopause Matter? Circ Research 2022 Jan 6: 130(3)



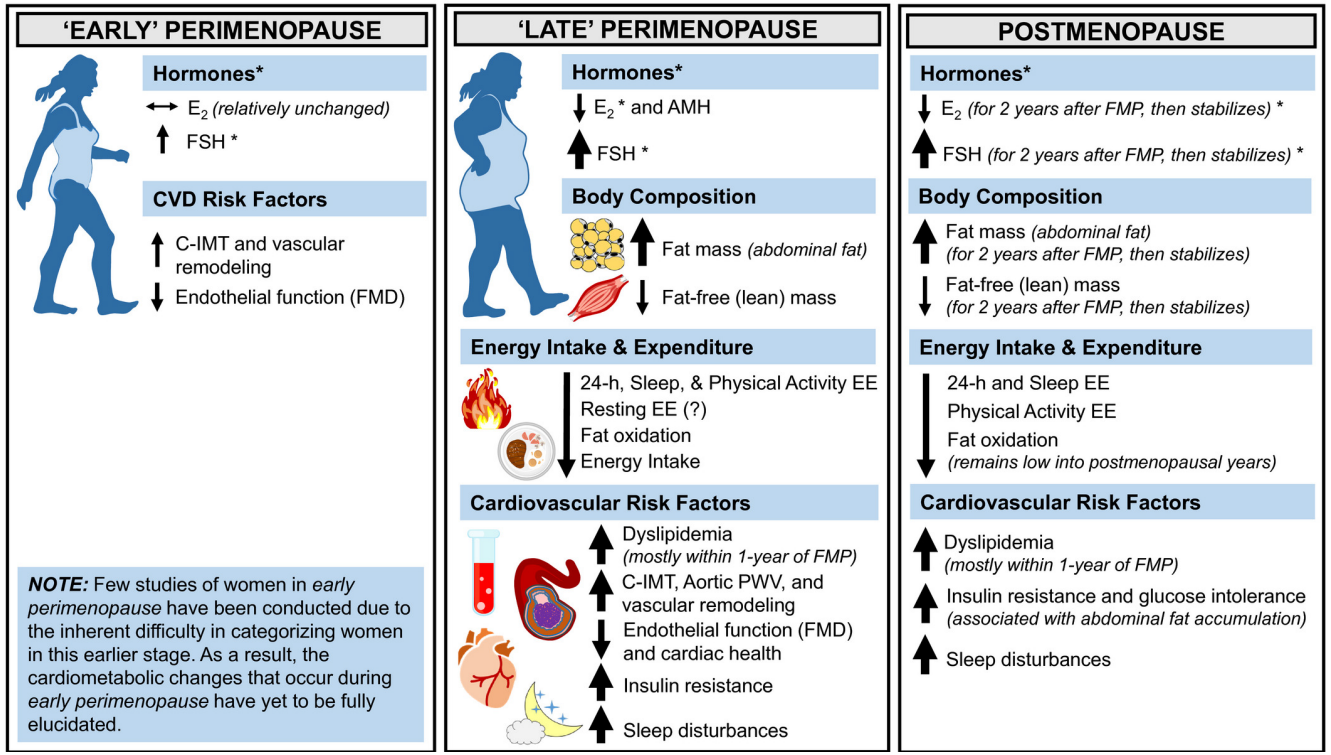
Clinical Endocrinology, Volume: 104, Issue: 6, Pages: 539-555, First published: 05 September 2025, DOI: (10.1111/cen.70027)

PALPITATIONS AND MENOPAUSE

- Palpitations effect 42% of perimenopausal and 54% of post menopausal woman and are associated with worse sleep, depression, stress and QOL
- 3 trajectories-survey of women reporting if they experienced heart pounding/racing or not in past 2 weeks
  - High probability palps periM diminish late postM (15.9% blue line)
  - Moderate probability of palps in periM diminishing in late postM (34.3% green)
  - Sustained low probability (49.8% red line)
- Palpitations NOT associated with subclinical CVD (CIMT, ABI)
- Palpitations were associated with poor sleep, higher stress, and vasomotor symptoms
- **Clinical Pearl: If patient has complaint of palpitations ask about age of menopause as earlier menopause (before 40) associated with increased risk of Atrial Fibrillation compared to menopause >50**



Carpenter JS, Cortés YI, Tisdale JE, Sheng Y, Jackson EA, Barinas-Mitchell E, Thurston RC. Palpitations across the menopause transition in SWAN: trajectories, characteristics, and associations with subclinical cardiovascular disease. Menopause. 2023 Jan 1;30(1):18-27.



Obesity, Volume: 30, Issue: 1, Pages: 14-27, First published: 21 December 2021, DOI: (10.1002/oby.23289)

MENOPAUSAL HORMONE THERAPY

HISTORICAL PERSPECTIVE

- 40+ observational studies (pre-1991): MHT initiated near menopause → 30–50% reduction in CHD rates
- Building on the above data, clinical trials of secondary prevention for CHD (HERS [Heart and Estrogen/Progestin Replacement Study]) and stroke (Women's Estrogen for Stroke Trial) were conducted in the 1990s with average ages at baseline of 67 and 72 years, respectively. Neither of these trials found benefit with MHT.

	Observational Studies	Randomized Trials
Mean age or age range at enrollment (years)	30–55	>63
Time-since-menopause at HRT initiation (years)	<2	>10
Menopausal symptoms (flushing)	predominant	excluded
Duration of therapy (years)	>10–40	<7
Body mass index (mean, kg/m^2)	25.1	28.5

Hodis HN, Mack WJ. Menopausal Hormone Replacement Therapy and Reduction of All-Cause Mortality and Cardiovascular Disease: It Is About Time and Timing. Cancer J. 2022 May-Jun 01;28(3):208-223

WHI CONCLUSIONS

- HT did not prevent CVD, dementia or other chronic disease
- CEE +MPA increased risk of chd, stroke, PE, and breast cancer
- CEE alone increased risk of stroke but not breast cancer
- Reduced risk of hip fracture and diabetes and were effective for vasomotor symptoms
- Older women 60 or older or >10 years since menopause experienced higher absolute and relative risk of adverse cardiovascular and thromboembolic events
- Younger women age 50-59 or within 10 years of menopause experienced lower absolute risks, but no statistically significant cvd benefit was observed

Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal Hormone Therapy and Health Outcomes During the Intervention and Extended Post stopping Phases of the Women's Health Initiative Randomized Trials. *JAMA.* 2013;310(13):1353–1368

HERS

- RCT daily estrogen 0.625 mg plus MPA 2.5 mg on CVD outcomes in postmenopausal women with CAD
- Ages 55 to 80 y.o. mean 66.7 years old
- No overall reduction in risk of CHD events with HT vs placebo over 4.1 years
- Significant increase in CVD events during first year of HT (1.5X increase)
- Extended follow up to 6.8 years did not show reduction in CVD
- Increased risk of venous thromboembolism and gallbladder disease in the hormone group
- They looked at 86 subgroups and none had clear benefit or harm with HT

Grady D, Herrington D, Bittner V, et al. Cardiovascular Disease Outcomes During 6.8 Years of Hormone Therapy: Heart and Estrogen/Progestin Replacement Study Follow-up (HERS II). *JAMA.* 2002;288(1):49–57. doi:10.1001/jama.288.1.49

DOPS (DANISH OSTEOPOROSIS PREVENTION STUDY)

- Only RCT designed to study HRT in a cohort of recently postmenopausal women with similar characteristics to women in observational studies
- Oral estradiol alone in women with hysterectomy and combined with norethisterone acetate in women with an intact uterus
- Mean age was 50 years, powered and designed to look at fracture reduction not CVD.
- After 10 years of treatment, the MHT group had a 52% lower hazard of hospitalized heart failure, MI and death compared with reference group (HR, 0.48 [95% CI, 0.26–0.87]), and the effect on stroke was null.
  - Small event numbers
  - CVD was secondary outcome
  - Study not powered to detect CVD events

Mosekilde L, Hermann AP, Beck-Nielsen H, Charles P, Nielsen SP, Sørensen OH. The Danish Osteoporosis Prevention Study (DOPS): project design and inclusion of 2000 normal perimenopausal women. Maturitas. 1999 Mar 15;31(3):207-19. doi: 10.1016/s0378-5122(99)00006-7. PMID: 10340280.

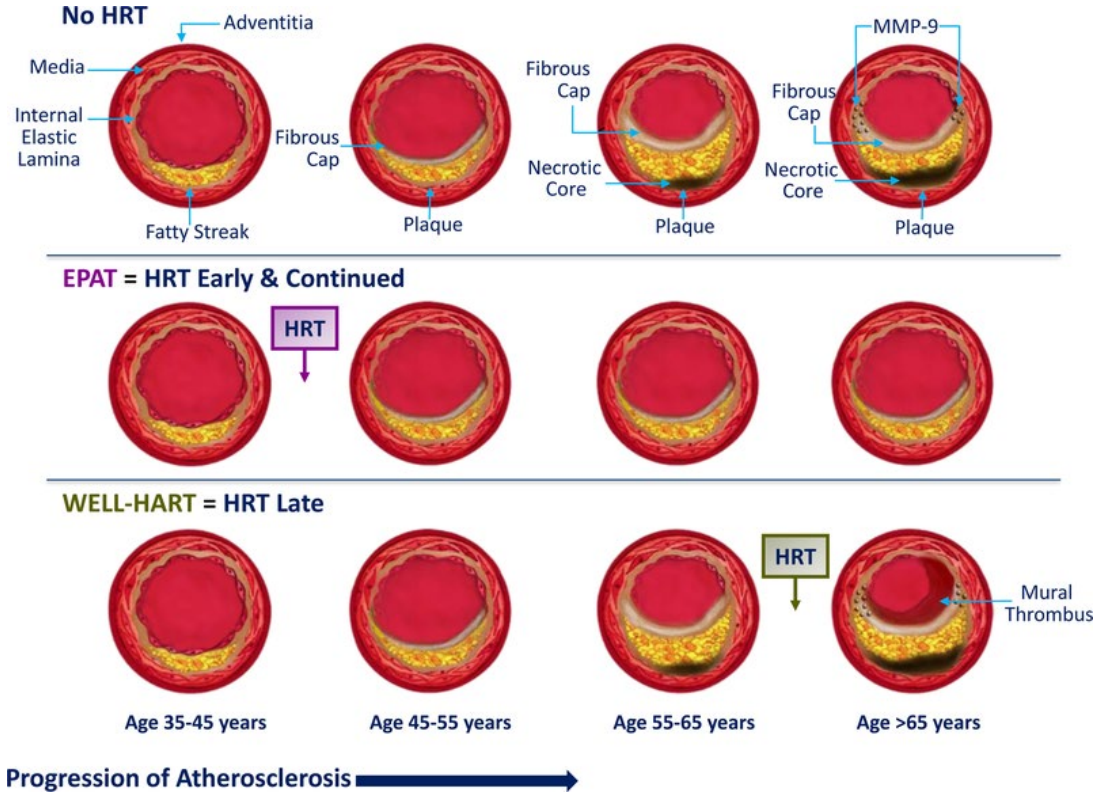
OBSERVATIONAL DATA FROM SWAN TRIAL

- Cohort data from SWAN trial looked at women with self reported vasomotor symptoms, free of CVT, no prior use of MHT
- Main outcome: CVD events (self reported), CVD related death from death certificates
- 2737 woman with vasomotor symptoms, 755 initiated MHT
- First trial to focus on younger women with vasomotor symptoms as criteria for MHT and CVD
- Key finding: MHT initiation in peri-menopausal and recently postmenopausal women with VMS contributed to a 22% reduction in CVD risk
- Unlikely to move guideline recommendations given not RCT but perhaps gives more clinician confidence in prescribing MHT to peri/post menopausal women with vasomotor symptoms

Wang Z, Swanson SA, Brooks MM, et al. Menopausal Hormone Therapy and Cardiovascular Risk in Midlife Women With Vasomotor Symptoms. *JAMA Intern Med.* Published online September 08, 2026.

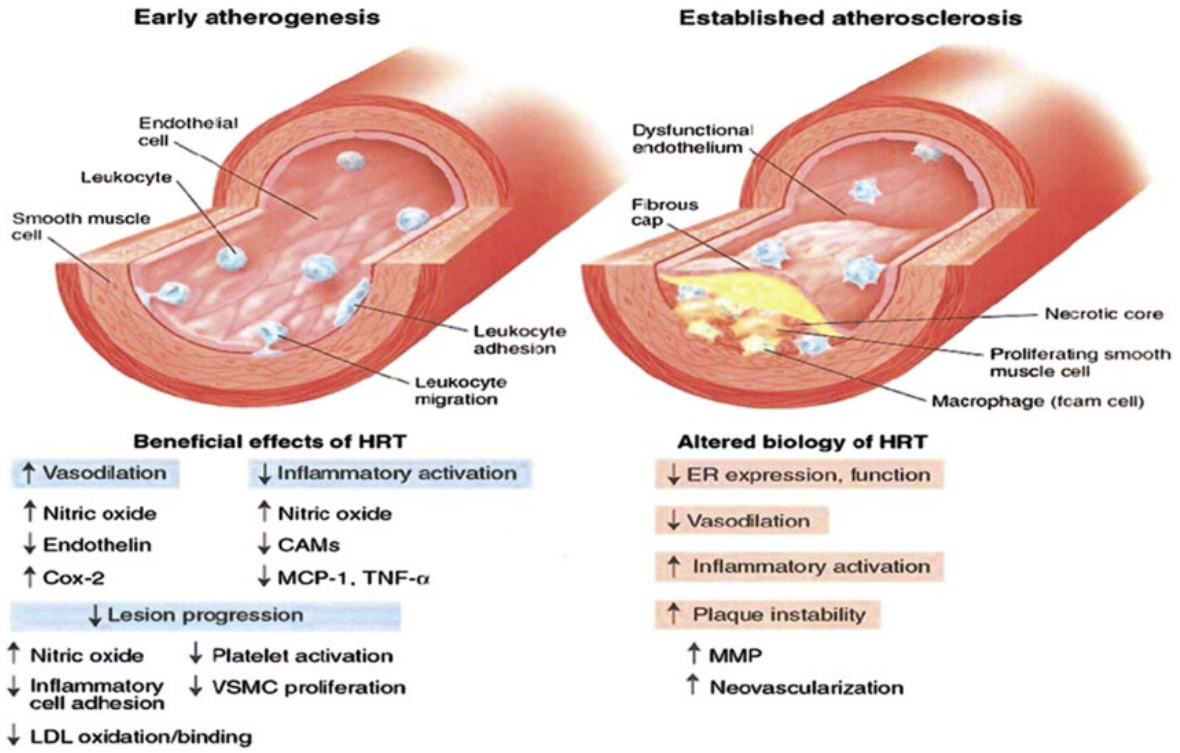
ESTROGEN DOES NOT REVERSE ATHEROSCLEROSIS BUT MAY STABILIZE IF STARTED EARLY

- EPAT: post menopausal no vascular disease, carotid wall evaluation, 60% on statins, no estrogen effect on atherosclerosis progression, estrogen showed reduction in progression of atherosclerosis compared to placebo
- WELL-HART: post menopausal women with vascular disease on statins, looked at angiograms, no estrogen/HT effect on disease, no increased risk of coronary events in the first year of use



Hodis HN, Mack WJ. Menopausal Hormone Replacement Therapy and Reduction of All-Cause Mortality and Cardiovascular Disease: It Is About Time and Timing. Cancer J. 2022 May-Jun 01;28(3):208-223

HRT EFFECT ON ATHEROSCLEROSIS



Tjoe B. Curr Treat Options Cardio Med (2021) 23:37

EARLY VS LATE INTERVENTION TRIAL WITH ESTRADIOL (ELITE)

- Only RCT specifically designed to formally test the HRT timing hypothesis in women who were randomized <6 years and >10 years since menopause, primary endpoint was change in CIMT measured every 6 months, a secondary endpoint was coronary atherosclerosis by cardiac CT, assessed at the end of treatment
- Oral estradiol slowed CIMT progression only when started within 6 years of menopause, not when started ≥10 years out
- Coronary CT measures (calcium, stenosis, plaque) did not differ between estradiol and placebo in either stratum

Hodis HN, et al. NEJM 2016;374:1221-1231

TIMING OF HT INITIATION

- Timing hypothesis
  - There may be less risk associated with HT use and potential CHD benefit if initiated closer to the time of menopause
  - In contrast, HT use initiated further from menopause may be harmful
- Evidence from the WHI
  - Absolute risk of CHD was lower in younger, recently postmenopausal women
  - Use of HT within 10 year of the onset of menopause was associated with a lower CHD risk than if it was started ≥ 20 years from LMP
  - Early Estrogen Prevention Study and the Early Versus Late Intervention Trial with Estradiol also showed safety of HT use initiated early in menopause

1. Evaluate age, time since menopause, and symptoms

<10 year from final menstrual cycle, <60 years old, and bothersome vasomotor symptoms

2. Perform ASCVD risk assessment and exclude HT contraindications

ASCVD risk factors

- Hyperlipidemia
- Hypertension
- Diabetes
- Family history of premature CVD in first-degree relative (men <55 or women <65 years of age)
- Obesity (BMI >30 kg/m^2)
- Physical inactivity
- Cigarette smoking
- Coronary calcification (moderate risk: CAC 1-99; high risk: CAC >100)
- History of preeclampsia
- History of systemic autoimmune collagen-vascular disease (e.g., lupus, rheumatoid arthritis)

Contraindications to systemic HT:

Coronary heart disease, stroke, TIA
Breast or endometrial cancer
History of pulmonary embolus, venous thrombosis or clotting disorder
Active liver disease
Undiagnosed abnormal vaginal bleeding

3. Evaluate risk category

May consider HT	***May consider HT, transdermal formulation***	***Not recommended to use HT:***
ASCVD risk <5% (low risk) and ≤1 CVD risk factor	ASCVD risk 5-10% or ASCVD risk <5% but ≥2 CVD risk factors	Age ≥60 or >10 years since menopause onset or ASCVD risk >10%

4. Ensure routine follow-up with re-evaluation of risks and benefits



Anna C. O'Kelly. Circulation Research. Pregnancy and Reproductive Risk Factors for Cardiovascular Disease in Women, Volume: 130, Issue: 4, Pages: 652-672, DOI: (10.1161/CIRCRESAHA.121.319895)

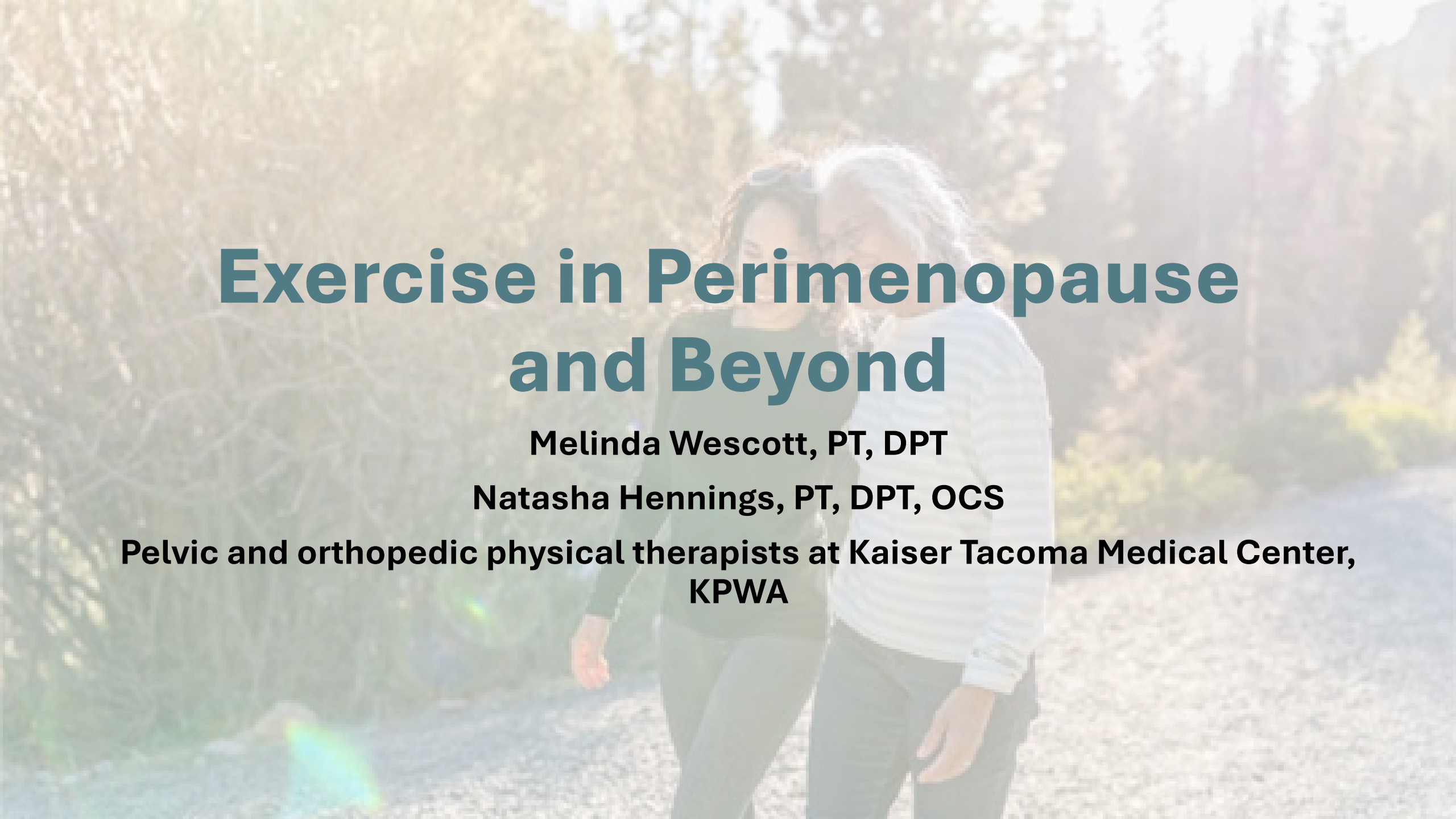
© 2022 American Heart Association, Inc.

ESTROGEN PREPARATIONS

- WHI observational study (n=93,676; 1994–2009): compared CVD outcomes across estrogen regimens
- Nonsignificant trends for lower rates of CHD, stroke, and CVD mortality, but not all-cause mortality, were reported for transdermal estradiol compared with oral CEEs.
- In a US matched-cohort study of health insurance claims between 1999 and 2011, transdermal estrogen preparations were associated with a lower incidence of CVD complications compared with oral estrogen preparations (incidence rate ratio, 0.81 [95% CI, 0.67–0.99]), regardless of the type of estrogen agent used.
- Most recently, 2 large nested case-control studies using the QResearch and Clinical Practice Research Datalink database in the United Kingdom evaluated the associations between various MHT regimens and the risk of venous thromboembolism. Oral MHT preparations were associated with increased venous thromboembolism, whereas transdermal preparations were not.
- CEE was associated with a higher risk than estradiol.
- Observational data indicates vaginal estrogen is not associated with increased CHD
- Low dose vaginal estrogen formulations are associated with minimal systemic absorption and are considered safe for GU symptoms without increasing CVD risk

KEY TAKEAWAYS

- When evaluating a woman's risk for CVD incorporate reproductive risk into your shared decision-making conversation around prevention therapies
- Menopause is a cardiovascular inflection point
- Estrogen decline worsens vascular and lipid risk
- Hormone therapy is not recommended for prevention of cardiovascular disease
- Timing determines whether HT helps or harms from a cardiovascular perspective
- Shared decision making is key to treating cardiovascular risk as well as determining if and when HT should be used in any given patient



Exercise in Perimenopause and Beyond

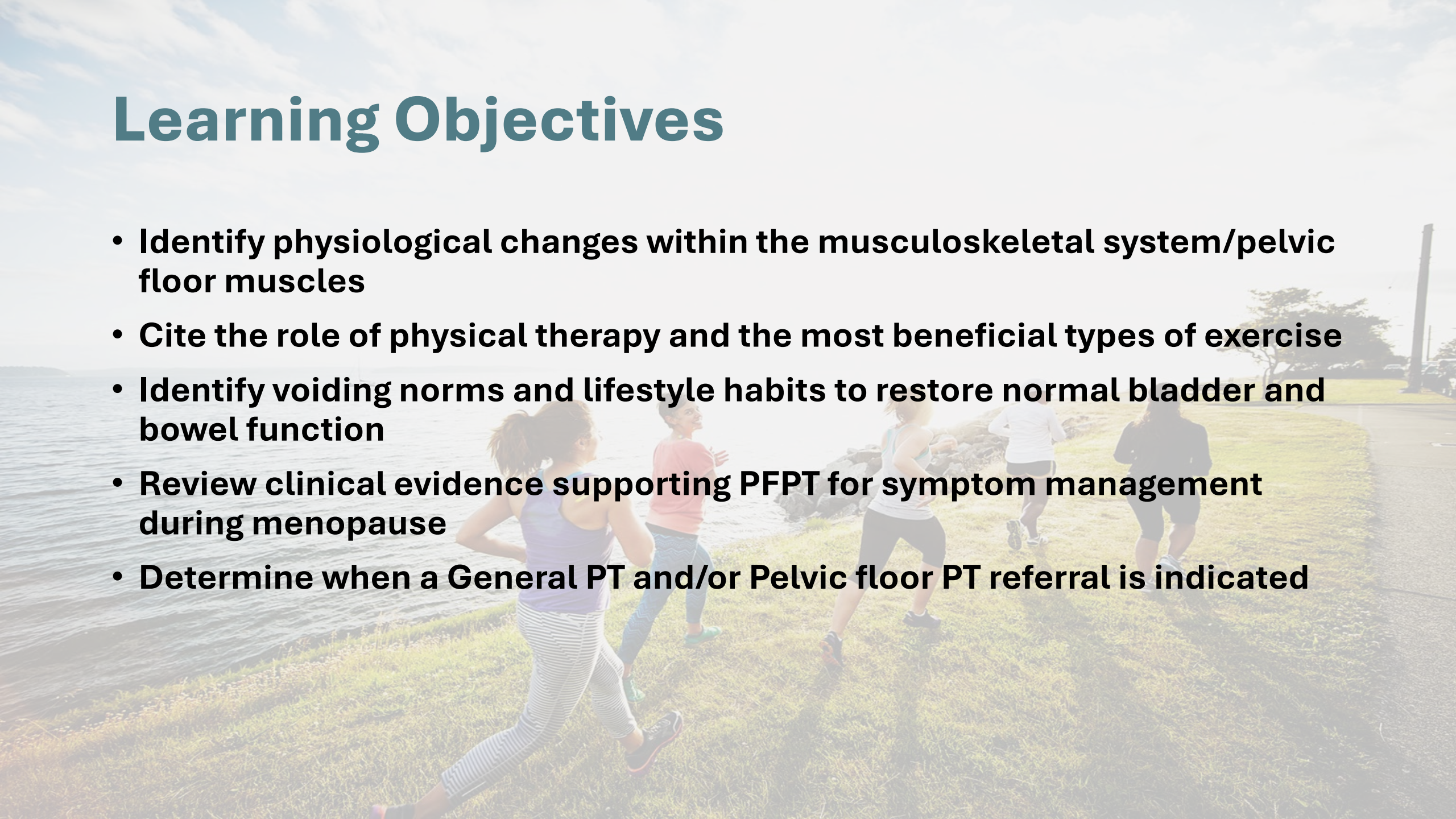
Melinda Wescott, PT, DPT

Natasha Hennings, PT, DPT, OCS

Pelvic and orthopedic physical therapists at Kaiser Tacoma Medical Center, KPWA

Learning Objectives

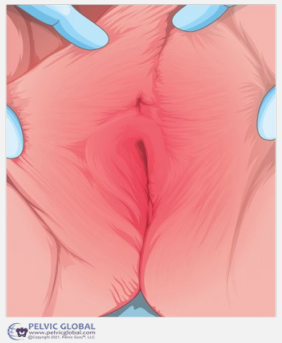
- Identify physiological changes within the musculoskeletal system/pelvic floor muscles
- Cite the role of physical therapy and the most beneficial types of exercise
- Identify voiding norms and lifestyle habits to restore normal bladder and bowel function
- Review clinical evidence supporting PFPT for symptom management during menopause
- Determine when a General PT and/or Pelvic floor PT referral is indicated



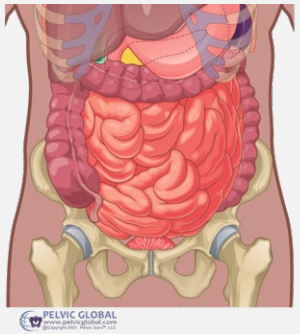
Physiological Changes

- Sarcopenia – 20-30% loss of muscle mass
- Tendonitis
- Systemic inflammation - joint pain
- Decreased bone density
- Cardiac changes

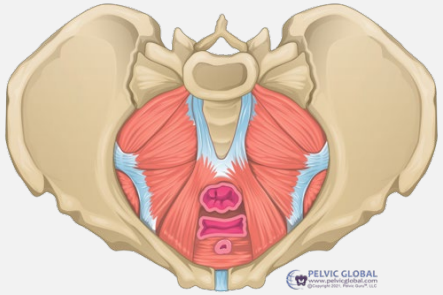
Physiological Changes – Pelvic Region



Tissue changes



Bowel function



Pelvic floor muscle weakness

General Benefits of Exercise



Increase muscle mass



Increase bone density



Decrease blood pressure/cholesterol



Increase metabolic rate



Increase insulin sensitivity

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Exercise: HIIT and SIT

HIIT

- Work at 80-95% effort for 45 seconds to 4 minutes
- 1:1 work to rest ratio
- Moderate recovery

SIT

- Work at MAX effort for up to 30 seconds
- Rest 30 seconds to 4 minutes
- Complete recovery



Other exercise



Role of the Pelvic Floor



Support bladder, urethra, rectum



Sphincteric control



Posture



Contract and relax during sexual activities

Pelvic Floor Muscle Exam

- **Exam options**
- **When you refer to pelvic PT give them a head's up?**

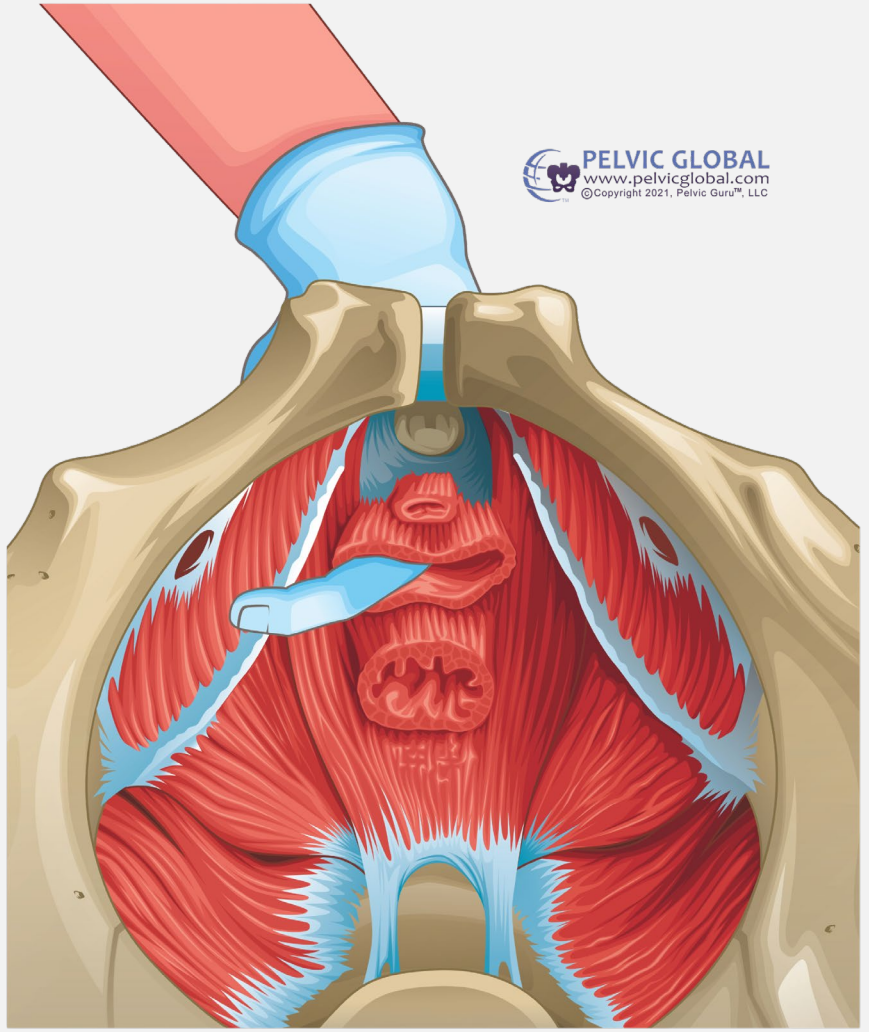
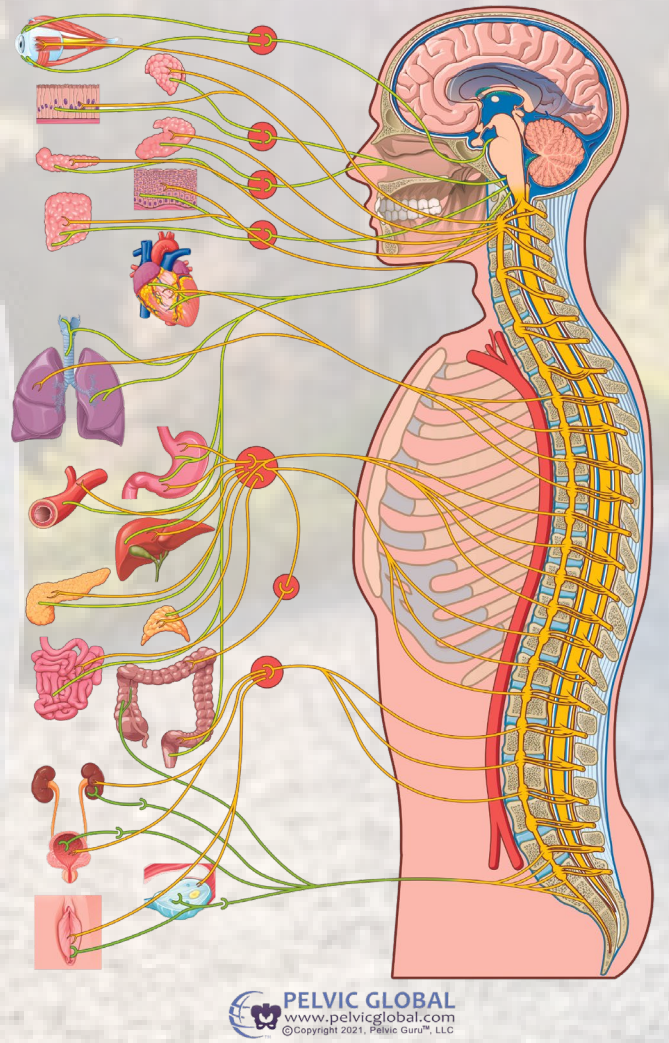


Image used with permission from Pelvic Guru®, LLC as a Pelvic Global Member

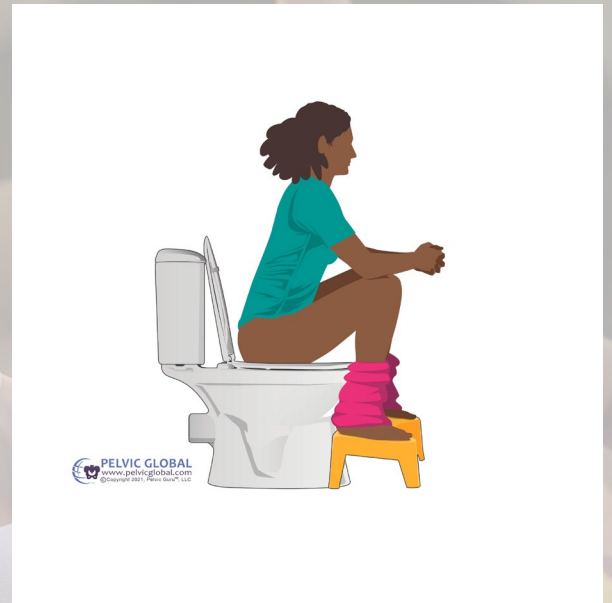
Pelvic Floor PT: Findings/Treatment

- Findings on pelvic exam
  - Tight/tender muscles
  - Weak muscles
  - Uncoordinated muscles
- Holistic
  - Educate on norms
  - Anatomy
  - Lifestyle factors
- Check other orthopedic connections
- Refer to specialties



General Behavioral Strategies for Optimal Bowel/Bladder Function

- ⬆ Water intake 8-10 glasses
- ⬇ Bladder irritants
- ⬆ Fiber intake 25-35 grams



Behavioral Strategies – Urinary Urge

- **Bladder re-training**

  ↑ **time in between voiding**

- **Specific techniques with urge:**
  - **Kegels, breathing, distraction**
  - **Heel raises**
  - **TTNS**



The Research

- **AUA Guidelines: In patients with pelvic floor dysfunction/GSM, clinicians may refer to a PFPT (expert opinion)**

- **12-week PFMT resulted in significant improvement in bothersome GSM symptoms**
  - **Increased vaginal secretions and improved vaginal color**
  - **Significant reduction in GSM signs/symptoms ($p < 0.01$)**
  - **Impact on ADL's, QOL, sexual function ($p < .05$)**

Mercier, J., Morin, M., Zaki, D. et al.: Pelvic floor muscle training as a treatment for genitourinary syndrome of menopause: A single-arm feasibility study. Maturitas, 125: 57, 2019

The Research

- **Systematic review of RCT's that evaluated the effect of targeted PFM exercise in post menopausal women for the treatment of UI**

- **Significant improvements in PFM strength, QOL, and severity of urinary incontinence**

López-Pérez MP, Afanador-Restrepo DF, Rivas-Campo Y, et al. Pelvic floor muscle exercises as a treatment for urinary incontinence in Postmenopausal Women: A systematic review of randomized controlled trials. Healthcare (Basel, Switzerland).January 11, 2023.

PT Referral

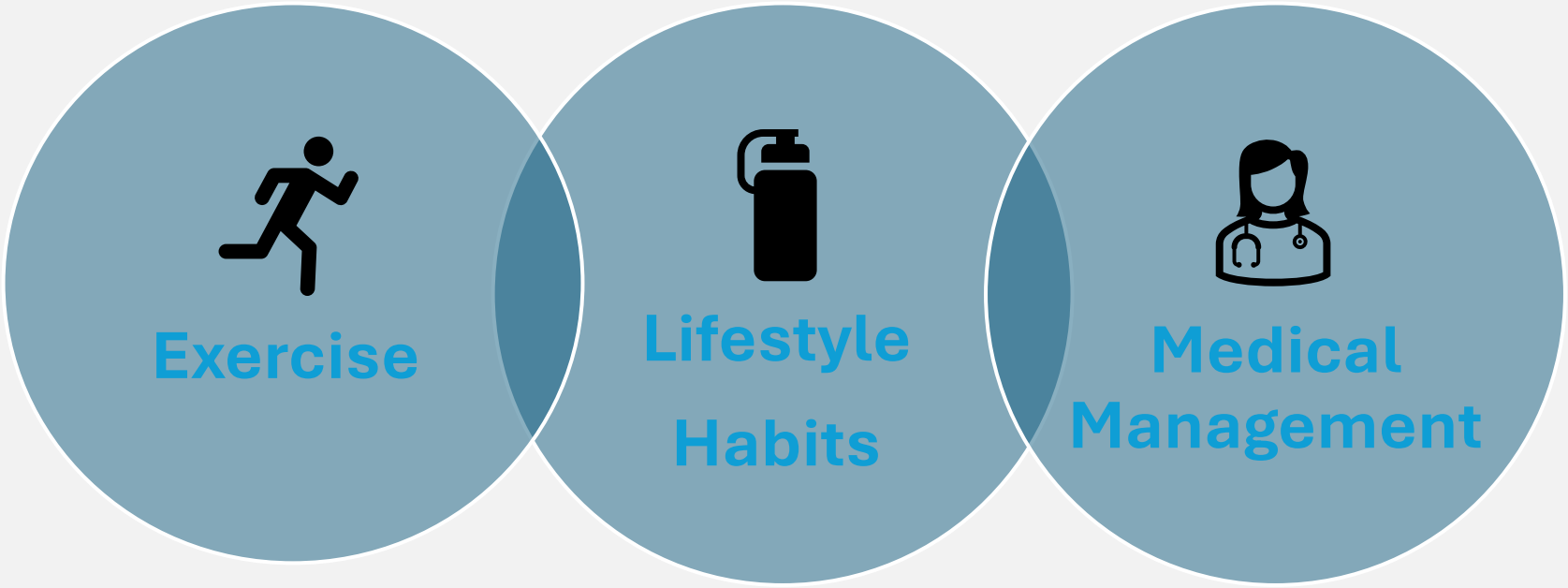
Pelvic PT:

- **Pelvic pain/ sexual dysfunction**
- Abdominal, hip, or back pain
- Urinary frequency/urgency
- Nocturia
- **Incontinence of bowel or bladder**
- Bowel concerns
- **Endometriosis or PCOS/PMOS history**
- Pre and post pelvic/abdominal surgery
- **Genitourinary syndrome**
- Pelvic organ prolapse

General PT:

- Joint /tendon pain
- Frozen shoulder
- **Hot flashes**
- **Dexa scan/Osteopenia**
- Feeling weak, loss of power
- Body changes

In Summary




Thank You!
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Nutrition for Perimenopause and Beyond

Nicole Merriam, MS, RD, CDCES

September 24, 2026

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Objectives

Identify limitations of weight ways to reduce weight stigma

Identify general nutrition gaps and recommendations for people in perimenopause

Identify specific diets that would be appropriate for perimenopause

Discuss concise actionable nutrition advise that will improve diet quality

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The purpose of nutrition

The goal of nutrition in menopause is to support overall health and wellness by reducing risk of heart disease, diabetes, and cancer. Additionally, nutrition should support bone and muscle retention to ensure independent living into older adulthood.

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Agenda

- Weight
- Reducing health risks with nutrition
- Bringing it all Together
- Resources for patients

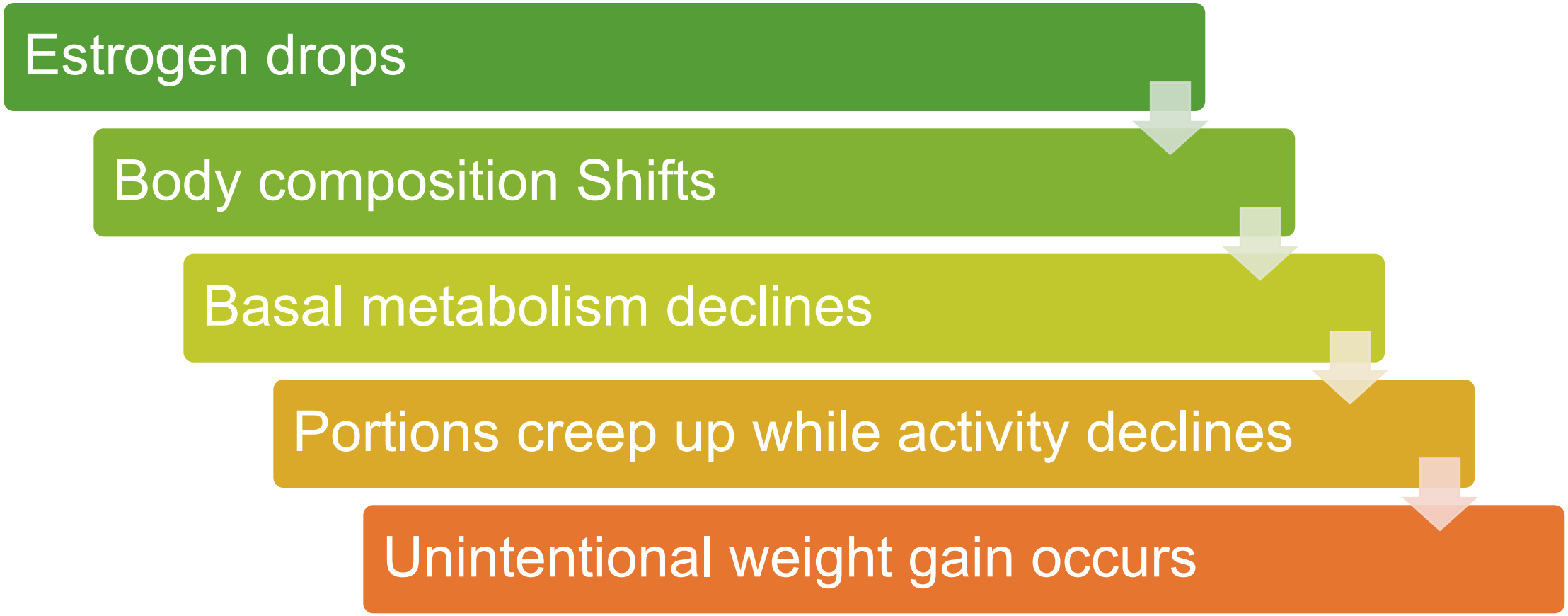
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Weight

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Body Changes



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Discussing Weight

Consider not talking about weight unless the patient brings it up

Do not assume you know someone's habits and lifestyle based on weight or BMI

Try to be specific with recommendations

There is no single diet plan that is more effective

Set realistic expectations – slower weight loss more likely

Focus on what can be ADDED not on what to RESTRICT

The best approach will build on what the patient is already doing

Knight, M. G., Anekwe, C., Washington, K., Akam, E. Y., Wang, E., & Stanford, F. C. (2021). Weight regulation in menopause. Menopause, 28(8), 960–965. https://doi.org/10.1097/GME.0000000000001792

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Health Behaviors Impact Health No Matter BMI



Those classified as fit, regardless of BMI status, showed no statistically significant increase in CVD or all-cause mortality risk compared with normal weight-fit individuals.

In contrast, all BMI classifications who were unfit showed twofold to threefold increases in risk of CVD and all-cause mortality compared with normal weight-fit individuals.

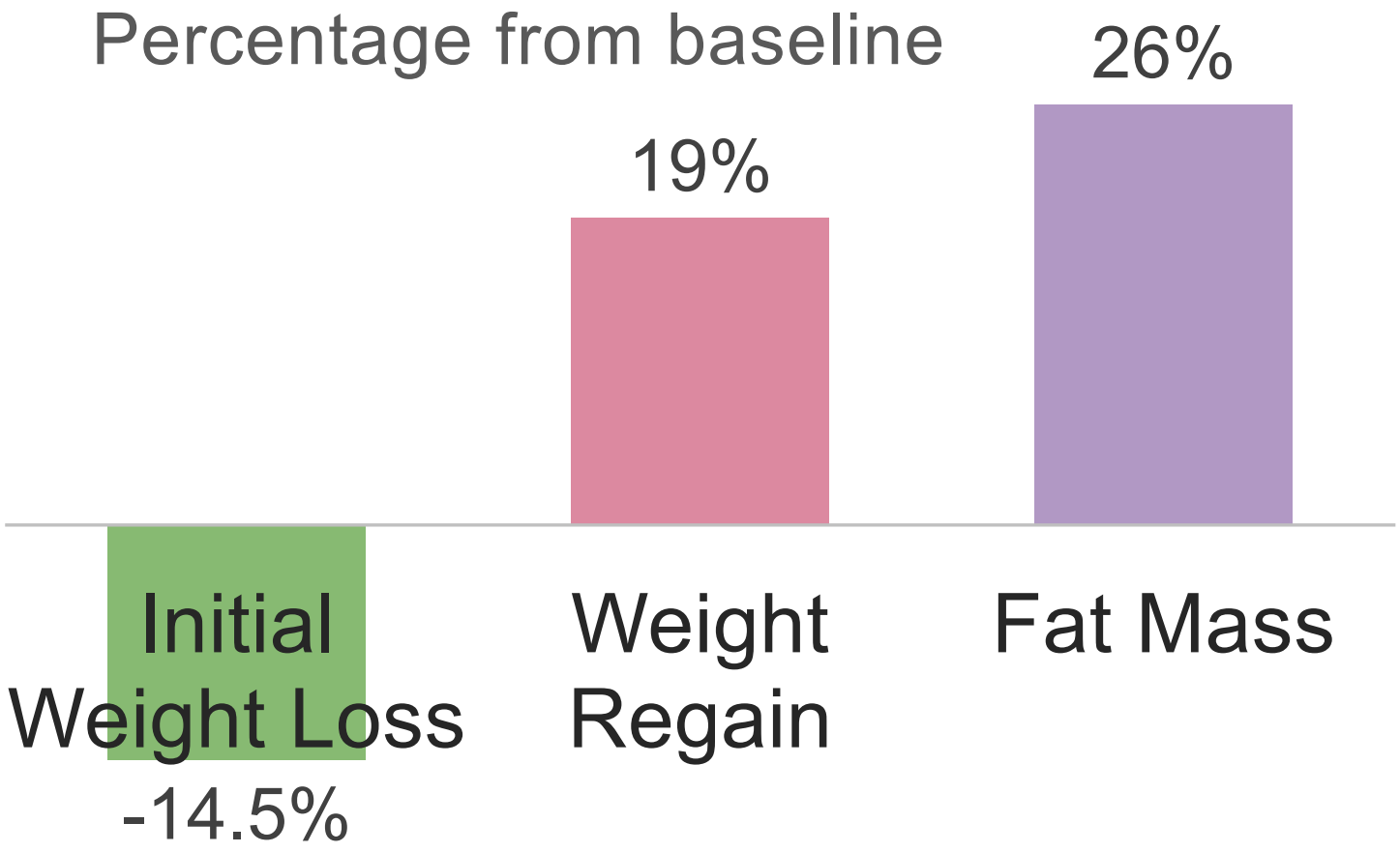
Reviewed studies included a greater proportion of females (33%) as well as a more globally diverse cohort compared with previous studies.

Weeldreyer NR, De Guzman JC, Paterson C, *et al* Cardiorespiratory fitness, body mass index and mortality: a systematic review and meta-analysis *British Journal of Sports Medicine* 2025;**59**:339-346.

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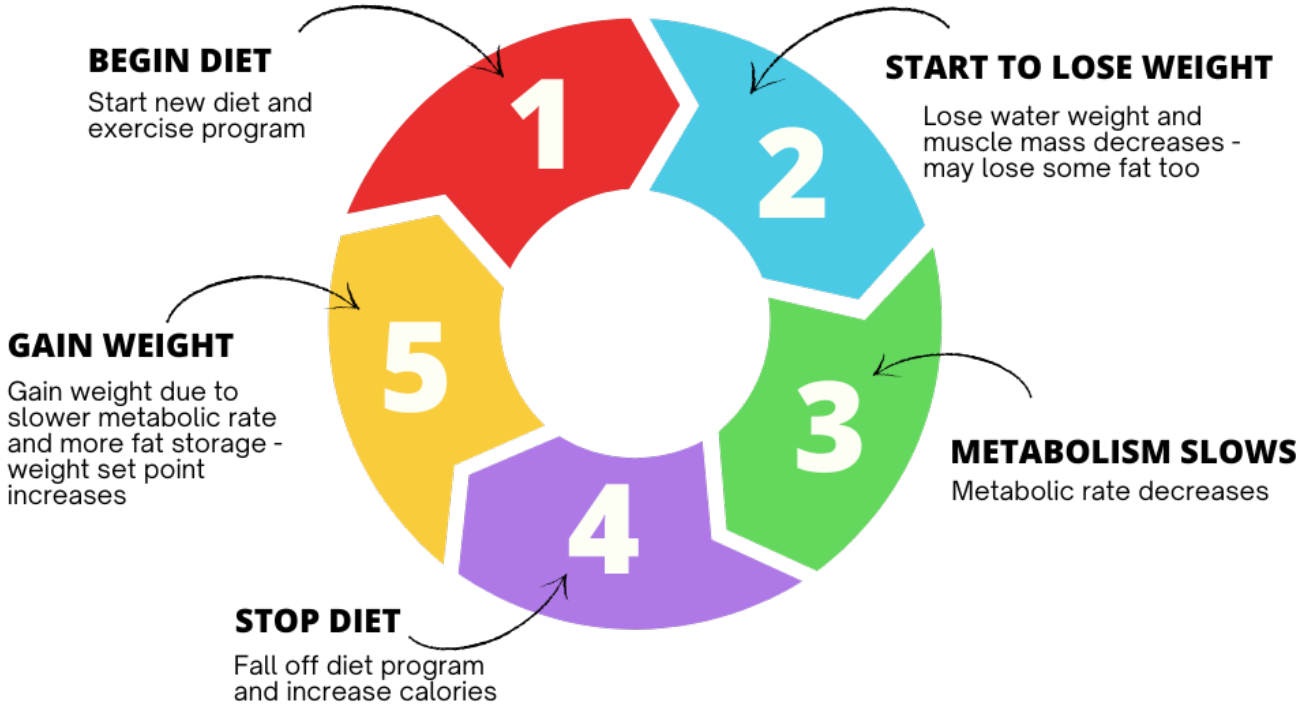
Weight cycling

Long-term outcomes of calorie restricting diets show one to two thirds of dieters regain more weight than lost



Strohacker K, Carpenter KC, McFarlin BK. Consequences of Weight Cycling: An Increase in Disease Risk? Int J Exerc Sci. 2009;2(3):191-201. doi: 10.70252/ASAQ8961. PMID: 25429313; PMCID: PMC4241770.
Mann T, Tomiyama AJ, Westling E, Lew AM, Samuels B, Chatman J. Medicare's search for effective obesity treatments: diets are not the answer. Am Psychol. 2007 Apr;62(3):220-33. doi: 10.1037/0003-066X.62.3.220. PMID: 17469900.

YO YO DIET CYCLE



Weight cycling increases the risk of cardiovascular disease, even when BMI is controlled.

Repeated dieting leads to metabolic slowdown, making weight loss harder over time.

Associations of weight gain from early to middle adulthood with major health outcomes later in life. *JAMA, 318(3), 255-269.*

The Toll of Weight Stigma

- Increased likelihood of depression, anxiety, suicidal thoughts, and low self esteem
- Increases in eating disorders related to internalized weight bias
- More likely to cancel appointments
- Avoidance of preventative care
- Increased inflammatory markers (CRP) and cortisol
- Lipid, and metabolic dysregulation
- Workplace discrimination

Fulton M, Dadana S, Srinivasan VN. Obesity, Stigma, and Discrimination. [Updated 2023 Oct 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554571/
O'Brien KS, Latner JD, Puhl RM, Vartanian LR, Giles C, Griva K, Carter A. The relationship between weight stigma and eating behavior is explained by weight bias internalization and psychological distress. Appetite. 2016 Jul 1;102:70-6. doi: 10.1016/j.appet.2016.02.032. Epub 2016 Feb 18. PMID: 26898319
Vadiveloo M, Mattei J. Perceived Weight Discrimination and 10-Year Risk of Allostatic Load Among US Adults. Ann Behav Med. 2017 Feb;51(1):94-104. doi: 10.1007/s12160-016-9831-7. Erratum in: Ann Behav Med. 2017 Feb;51(1):105. doi: 10.1007/s12160-016-9870-0. PMID: 27553775; PMCID: PMC5253095.

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What is the overall effect?

Assumes that people falling within the “healthy” BMI range are engaging in health promoting behaviors



People falling within the “healthy” BMI range fall through the cracks

Assumes that people outside the “healthy” BMI range are not engaging in healthy promoting behaviors

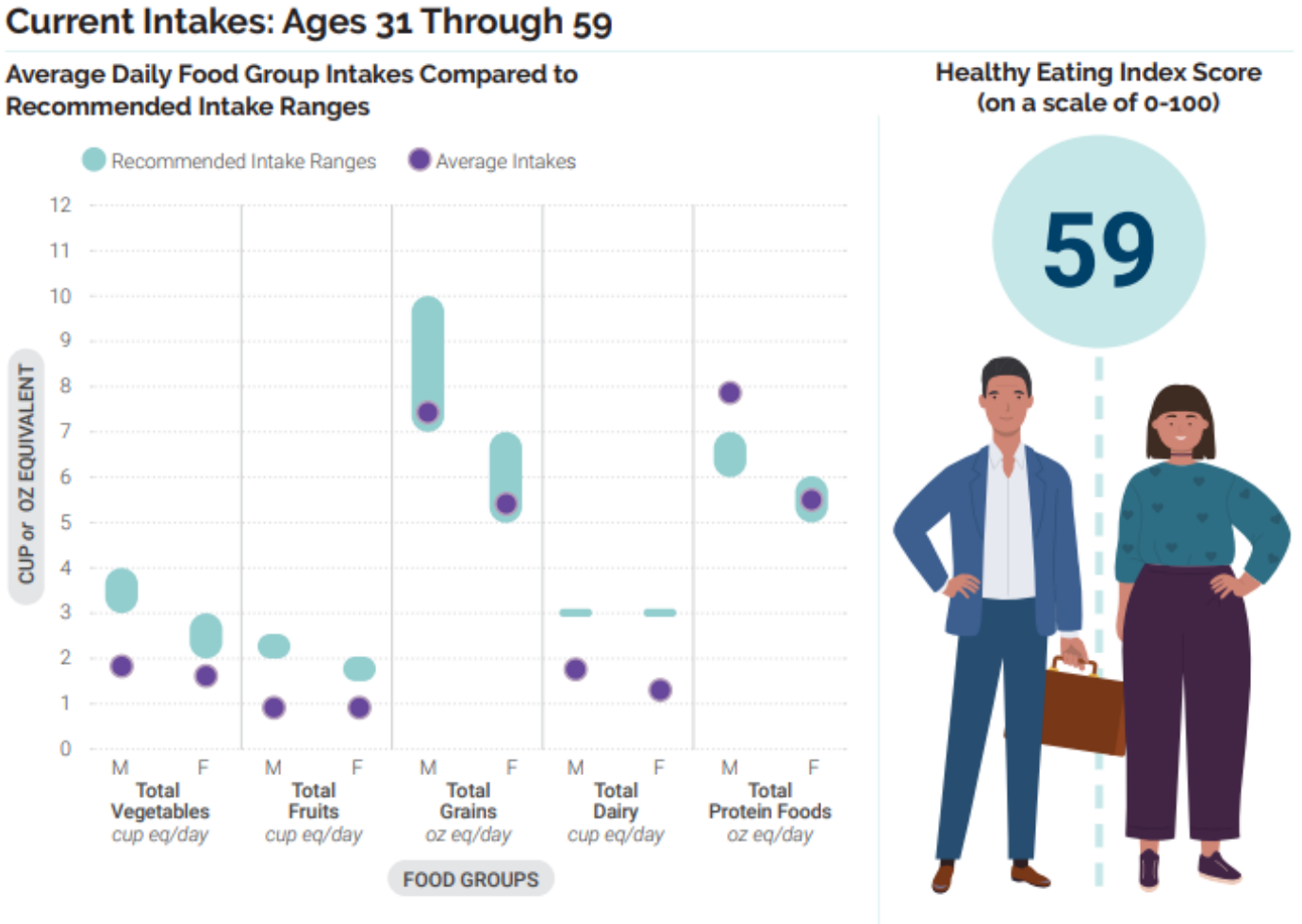


People above the “healthy” BMI range experience weight stigma

Reducing Risk of Chronic Disease

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Average Intake

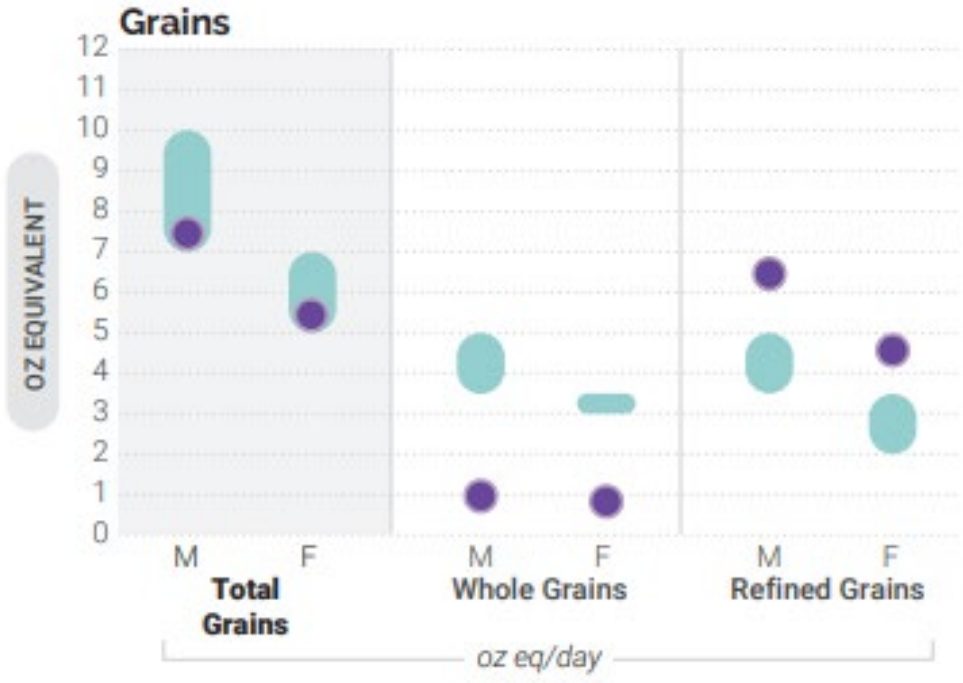


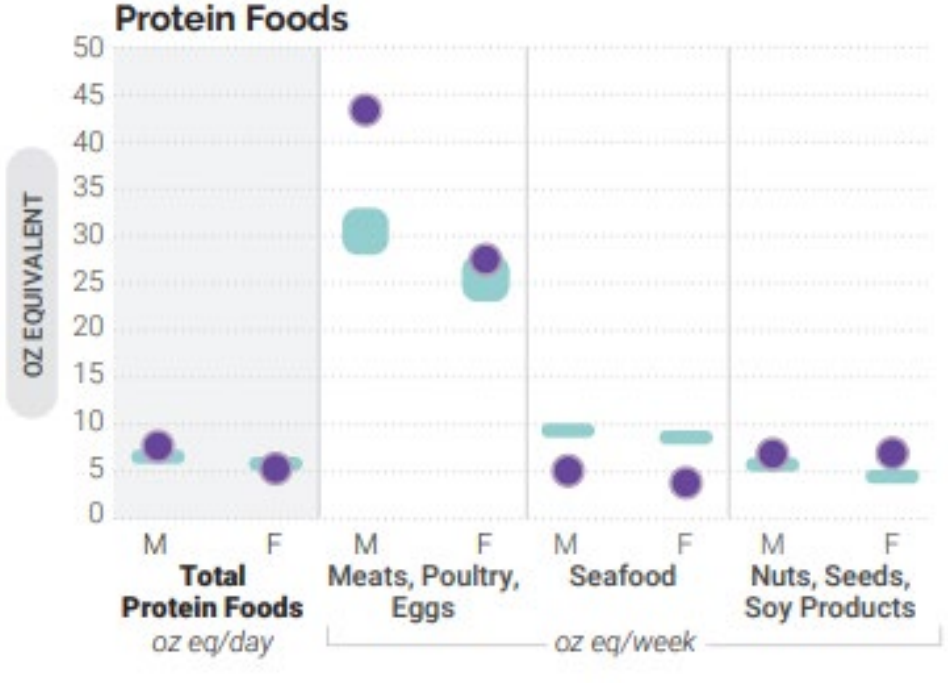
Data Sources: *Average Intakes and HEI-2015 Scores*: Analysis of What We Eat in America, NHANES 2015-2016, day 1 dietary intake data, weighted. *Recommended Intake Ranges*: Healthy U.S.-Style Dietary Patterns (see ***Appendix 3***). *Percent Exceeding Limits*: What We Eat in America, NHANES 2013-2016, 2 days dietary intake data, weighted.

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Taking a closer look





Data Sources: *Average Intakes*: Analysis of What We Eat in America, NHANES 2015-2016, day 1 dietary intake data, weighted. *Recommended Intake Ranges*: Healthy U.S.-Style Dietary Patterns (see ***Appendix 3***).

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Percent Exceeding Limits of Added Sugars, Saturated Fat, and Sodium

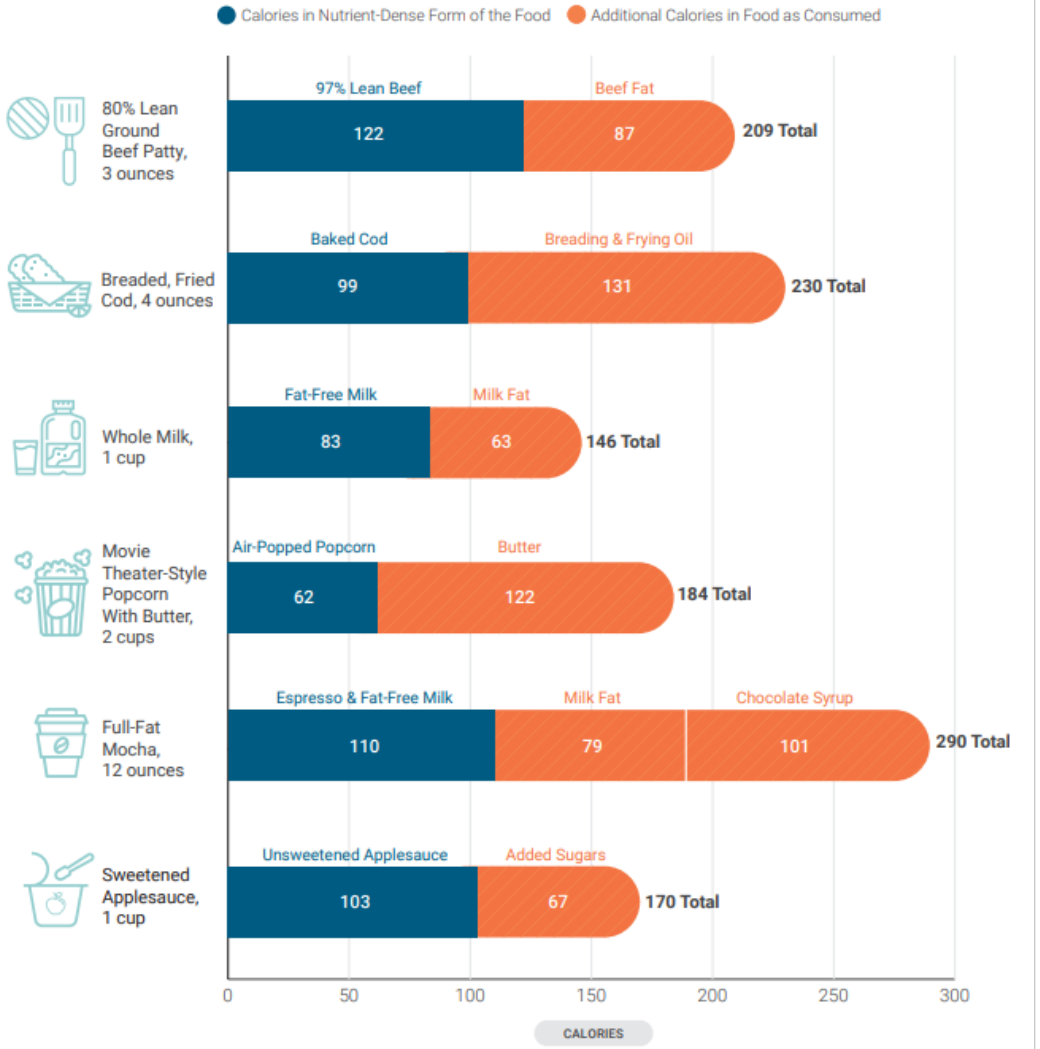


Data Sources: *Average Intakes and HEI-2015 Scores*: Analysis of What We Eat in America, NHANES 2015-2016, day 1 dietary intake data, weighted. *Recommended Intake Ranges*: Healthy U.S.-Style Dietary Patterns (see ***Appendix 3***). *Percent Exceeding Limits*: What We Eat in America, NHANES 2013-2016, 2 days dietary intake data, weighted.

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Examples of Calories in Food Choices That Are Not Nutrient Dense and Calories in Nutrient-Dense Forms of These Foods



Data Source: U.S. Department of Agriculture, Agricultural Research Service. FoodData Central, 2019. fdc.nal.usda.gov.

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Protein

Critical for maintaining bone and muscle mass

Needs increase to 1-1.2 g/kg/d (or 16% of total energy)

~80g of protein per day for most women



Silva, T. R., & Spritzer, P. M. (2017). Skeletal muscle mass is associated with higher dietary protein intake and lower body fat in postmenopausal women: a cross-sectional study. Menopause, 24(5), 502–509. https://doi.org/10.1097/GME.0000000000000793

Wright, H., & Ward, E. M. (2020). *The menopause diet plan: A natural guide to managing hormones, health, and happiness*. Rodale Books.

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Fiber

Most Americans are not meeting fiber targets

Plays a critical role in heart disease and type 2 diabetes management

Supports bowel health

Improves satiety

Target: 25-35g per day

Sources: whole grains, fruits, vegetables, nuts, sees, legumes, beans, chia seeds, flaxseed meal



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Bone Health

Calcium

1000-1200mg daily

Requires 3-4 servings of calcium rich foods daily

Most women would benefit from supplementation

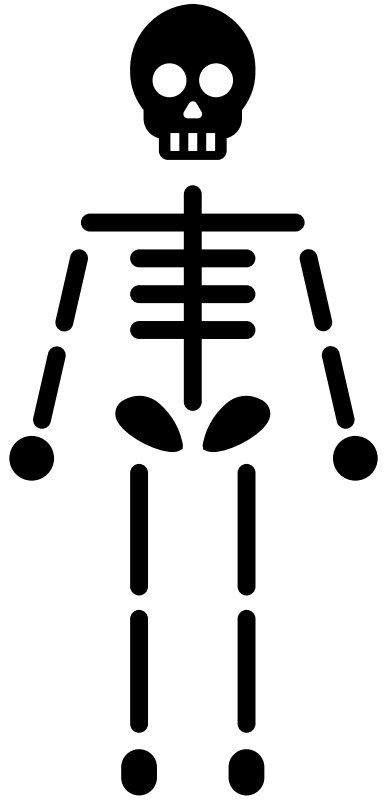
Vitamin D

600IUs daily

Difficult to obtain via diet alone

Recommend checking vitamin D status to help guide supplementation

1000-2000IUs for women with or at risk for osteoporosis



The North American Menopause Society. (2022). Postmenopausal osteoporosis (MenoNote). https://www.menopause.org

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Diet and Menopause

Diets that are pro-inflammatory are associated with more somatic symptoms

More energy dense diets are associated with increased somatic, psychological, and total menopause symptoms

Increased plant protein intake from soy is associated with a reduction in hot flashes

Diets with lower inflammatory potential in pre and perimenopause are correlated with fewer fractures later in menopause

Alcohol and consumption of spicy foods are associated with hot flashes

Diets higher in phytoestrogen may improve cardiovascular risk factors in some women

Barnard, N. D., Kahleova, H., Holtz, D. N., Znayenko-Miller, T., Sutton, M., Holubkov, R., Zhao, X., Galandi, S., & Setchell, K. D. R. (2022). A dietary intervention for vasomotor symptoms of menopause: a randomized, controlled trial. Menopause, 30(1), 80–87. https://doi.org/10.1097/GME.0000000000002080

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Specific Diets

DASH Diet

Emphasizes: vegetables, fruit, whole grains, low fat dairy products, lean meats, beans, and nuts

Limits: saturated fat, added sugars, sodium

Mediterranean Diet

Emphasizes: cold pressed olive oil, vegetables, fruits, nuts, beans, lentils, lean meats

Limits: added sugar, sodium, processed meats, refined carbohydrates

MIND Diet

Emphasizes: vegetables, nuts, berries, beans/legumes, fish, poultry, olive oil, whole grains

Limits: red meat, fried foods, fast food, sweets, butter, and cheese

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Bringing it All Together

KAISER PERMANENTE®

The Basics

Eat breakfast in the first hour to hour and a half of waking

Include 3 meals and snacks as needed to avoid going more than 4 to 5 hours without eating

Breakfast and snacks should include a high-quality carbohydrate and protein

Lunches and dinners should mirror the plate method

Incorporate more fish and plant-based proteins (tofu, beans, lentils)

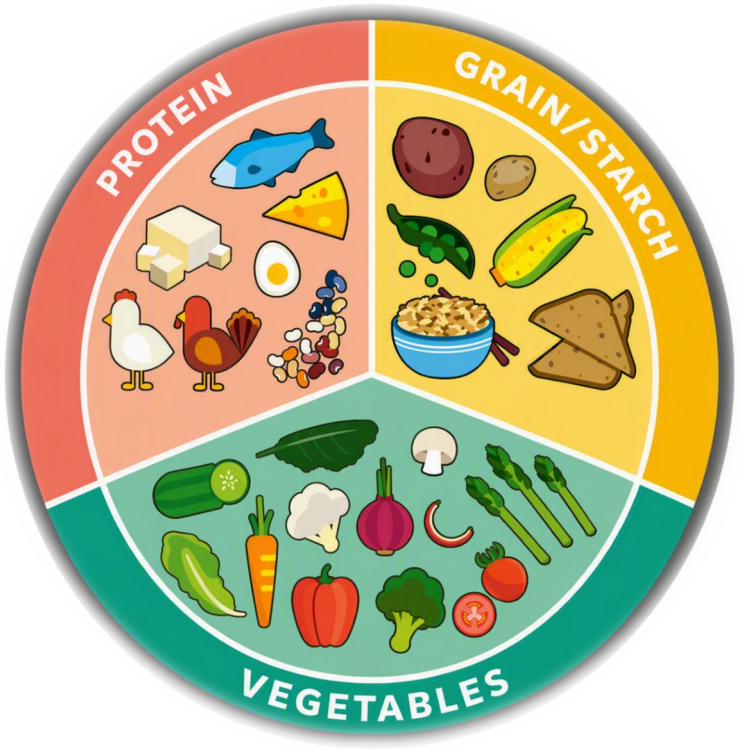
Choose low fat yogurt and cheeses

Recommend taking 500mg of calcium daily

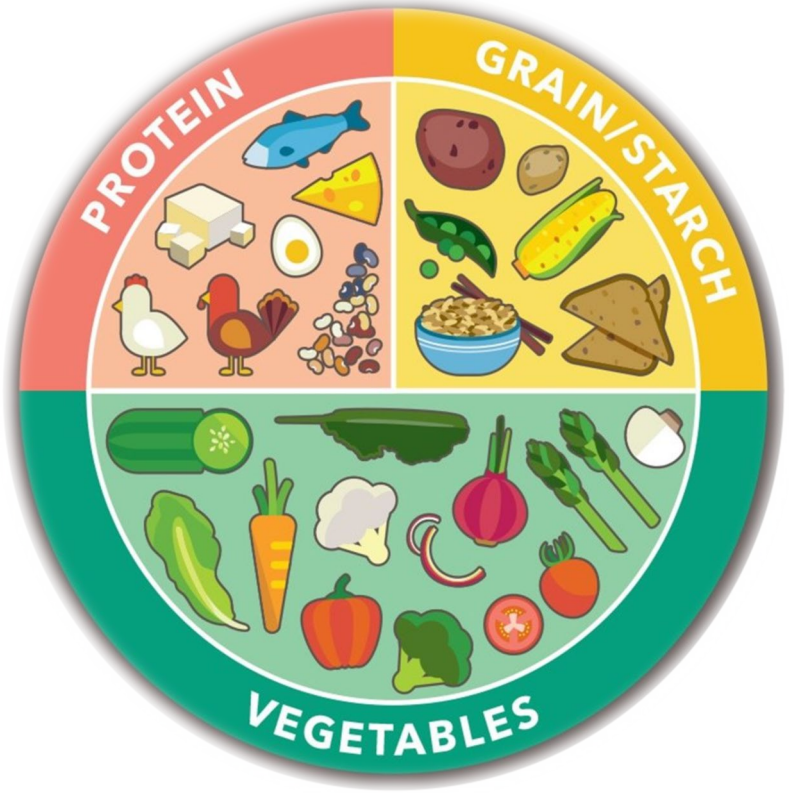
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Plate Method



3 meals per day



3 meals per day + snacks

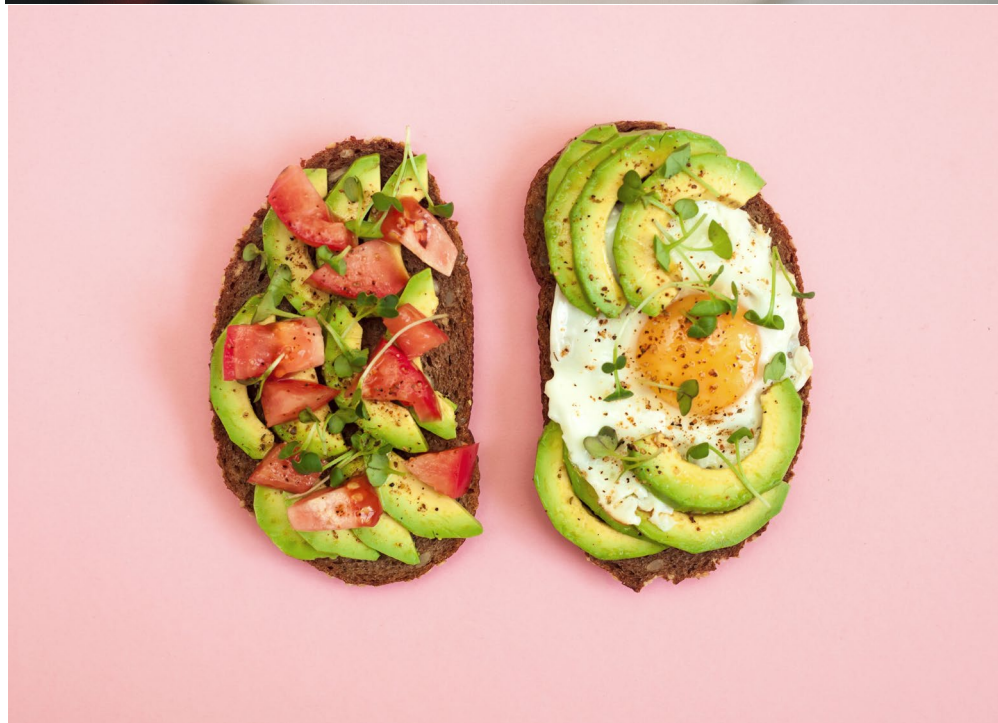
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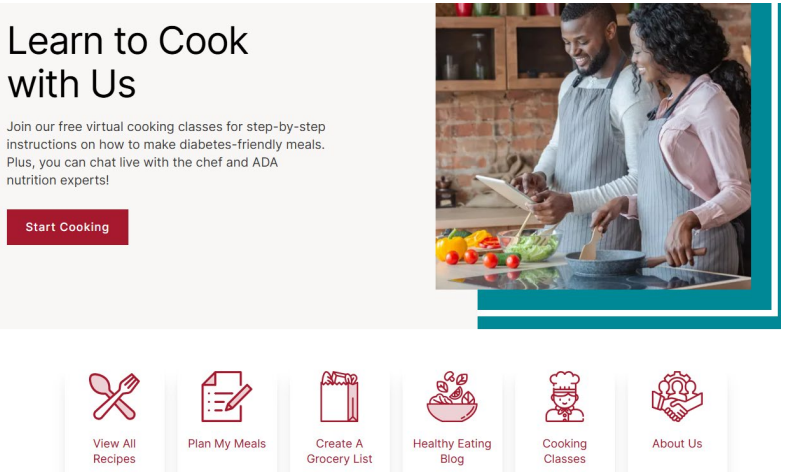
The plate pattern isn't the only option!

- Breakfast and snack do not always fit nicely into the plate pattern.
- Try including a **carbohydrate + protein + fiber** if not using the plate pattern.
  - The fiber part is typically a part of the carbohydrate or protein.
  - Examples
    - Fruit + cheese or nuts or nut butters
    - Whole grain cracker + cheese or nuts or nut butters
    - Hummus + carrots
    - Greek yogurt + fruit + nuts
    - Eggs + whole grain toast
    - Oatmeal + nuts + berries

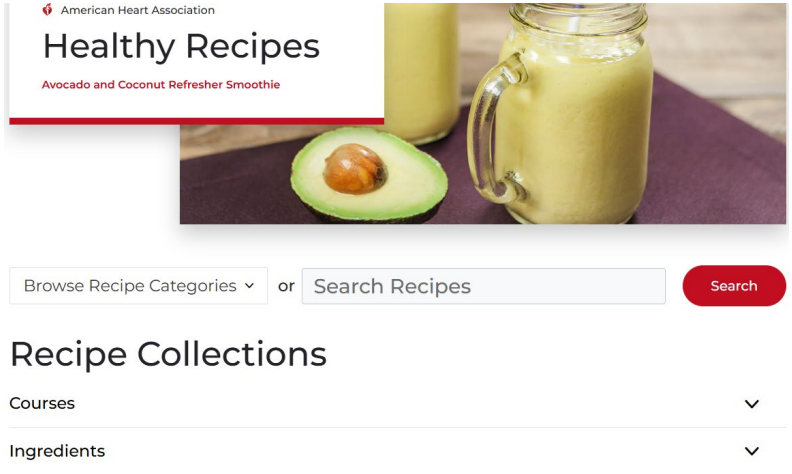




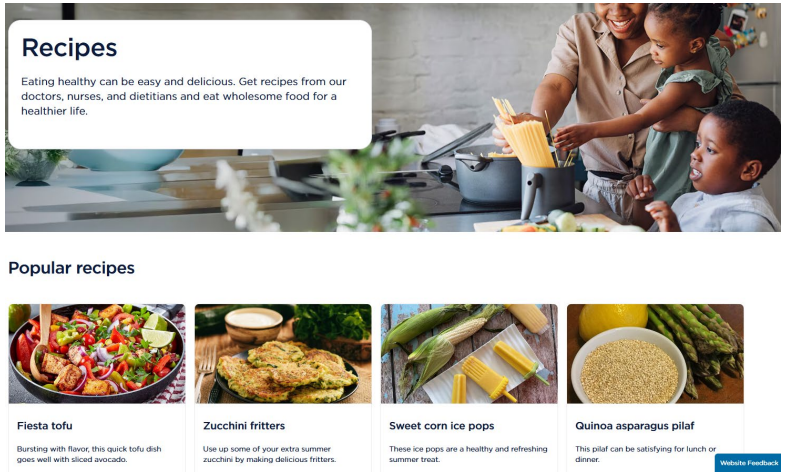
Cooking Resources



Diabetes Food Hub



American Heart Association



Kaiser Permanente

Available through KPW Nutrition Services

Classes

- Thriving on GLP-s: Nutrition Basics
- Foundations for Healthy Living
- Heart Healthy Nutrition
- Lifestyle Medicine
- Intuitive Eating
- Healthy Connections (a diabetes prevention program)



Thank you!

Nicole Merriam, MS, RD, CDCES
Nicole.x1.Merriam@kp.org or on Teams



Influencers, Algorithms, and “Menopause Clinics”

What Patients Are Hearing

Commercial incentives, clinical claims, and a trust-preserving response

Ory Holtzman, MD MBA FACOG MSCP

September 2026

TODAY

Learning objectives

Map the market

Describe how unmet need, attention, and investment created a rapidly expanding menopause marketplace.

Interrogate claims

Recognize recurring claims about testing, supplements, compounded hormones, testosterone, and pellets.

Follow incentives

Distinguish access innovation from revenue models that reward product stacking or high-friction discontinuation.

Preserve trust

Use a validating, evidence-based response that does not repeat the patient’s experience of dismissal.

MARKET FORMATION

Why menopause became a “gold rush”

Unmet need

Symptoms were often minimized; clinician training and access were inconsistent.

Attention shift

Social media, workplace advocacy, and changing interpretation of hormone therapy increased demand.

Commercial scale

Virtual care, subscriptions, supplements, diagnostics, and procedures created multiple revenue streams.

$26.6B

estimated annual U.S. burden including medical expenses and lost work time

$10–15B

2026 industry estimate of the current menopause market

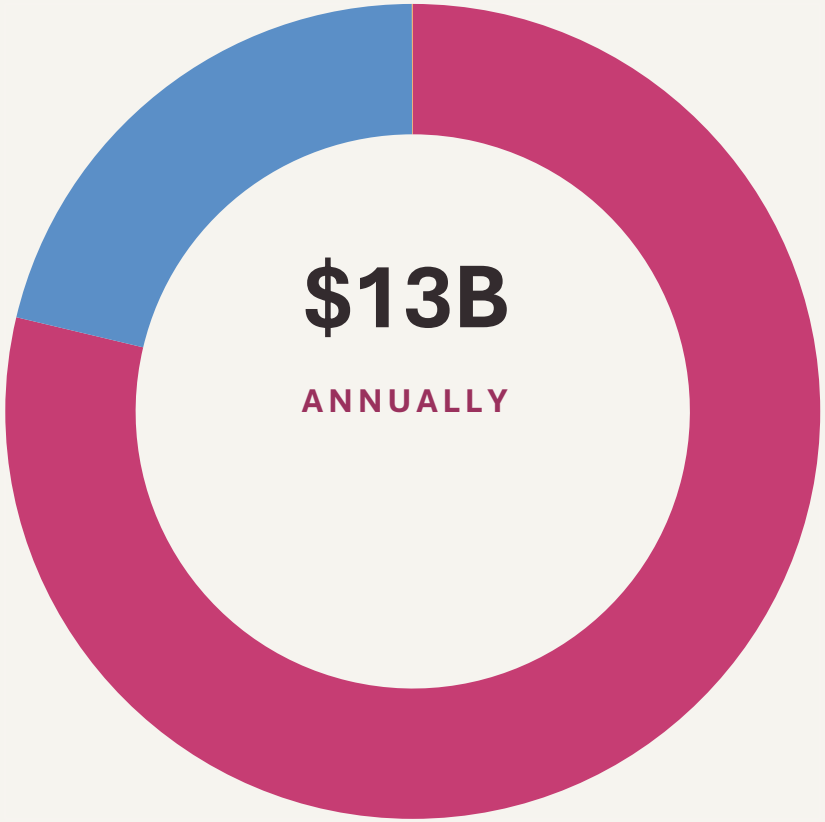
$15–25B

industry projection for 2030, not a clinical epidemiologic estimate

- Mayo Clinic News Network, 2023: https://newsnetwork.mayoclinic.org/discussion/mayo-clinic-study-puts-price-tag-on-cost-of-menopause-symptoms-for-women-in-the-workplace/
- Forbes citing PwC market analysis, 2026: https://www.forbes.com/sites/geristengel/2026/06/29/what-the-15-billion-menopause-market-doesnt-count/

Women spend $13 billion annually addressing menopause symptoms

Most spending is directed toward nonmedical options



$10B+

Nonmedical treatments

Supplements, OTC products and wellness solutions

$2.7B+

Hormone therapy

Prescription hormone replacement therapy

$4.5M+

Copays

Too small to display proportionally in the donut

Sauer J. *2023 AARP Employer Menopause Survey*.; 2023. doi:10.26419/res.00720.001

FUNDING EXAMPLES

Capital is moving into menopause care

EVERNOW

$28.5M

Series A

2022

ALLOY

~$21M

reported total raised

2026

MIDI

$100M

Series D

2026

MIDI

>$1B

company-reported valuation

2026

- Evernow funding announcement, 2022: https://www.prnewswire.com/news-releases/evernow-raises-28-5m-in-series-a-funding-to-redefine-menopause-treatment-301518212.html
- Midi Health company announcement, 2026: https://www.joinmidi.com/press-release/series-d-announcement
- Forbes profile of Alloy and Midi, 2026: https://www.forbes.com/sites/geristengel/2026/06/22/a-21-million-company-is-betting-against-the-250-million-race-in-menopause-care/

FOLLOW THE REVENUE STREAM

The care model shapes the incentive

Subscription model → Recurring revenue

Emphasis on supplements → Revenue not dependent on generic drug market

Pellet / procedure clinic → Prescriber sells pellet and charges procedure fee

Lab-driven optimization → Maintains patient engagement

ATTENTION ECONOMICS

The algorithm is not a neutral clinician



- Social platforms allow users to instantaneously publish on virtually any topic
  - Misinformation “goes viral”
  - Influencers build solidarity through subjective certainty and personal narrative
  - Distress-framed posts increase worry, confusion, and perceived knowledge at the same time.
  - Algorithms dictate content in a feed-forward cycle
  - Content creators and social media platforms are financially incentivized for publishing misinformation

- Visual on this slide was generated with Microsoft Copilot.
- Denniss & Lindberg, Health Promotion International, 2025: https://pmc.ncbi.nlm.nih.gov/articles/PMC11955583/
- Van Poucke, Atlantic Journal of Communication, 2025: https://www.tandfonline.com/doi/pdf/10.1080/15456870.2025.2453738
- Osborne et al., JMIR Formative Research, 2026: https://pmc.ncbi.nlm.nih.gov/articles/PMC13428204/

CLAIM → EVIDENCE CHECK

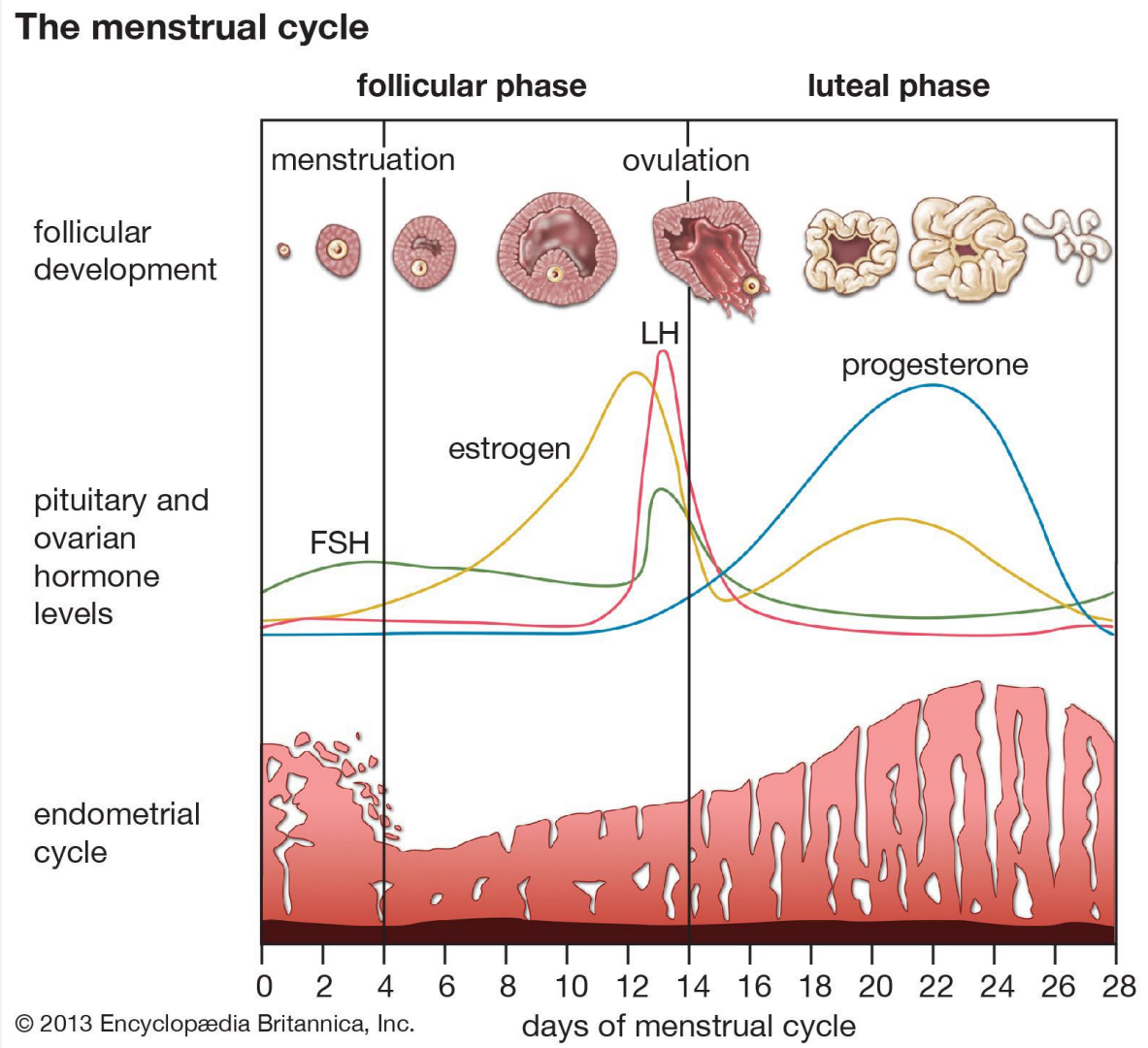
Common claims: start with the kernel of truth

“Conventional medicine does not understand menopause”

“A full hormone panel reveals what others missed”

“Bioidentical means natural and safer”

“Pellets give stable, optimized levels”



Menstrual Cycle. Encyclopedia Brittanica. https://www.britannica.com/science/menstrual-cycle

CLAIM → EVIDENCE CHECK

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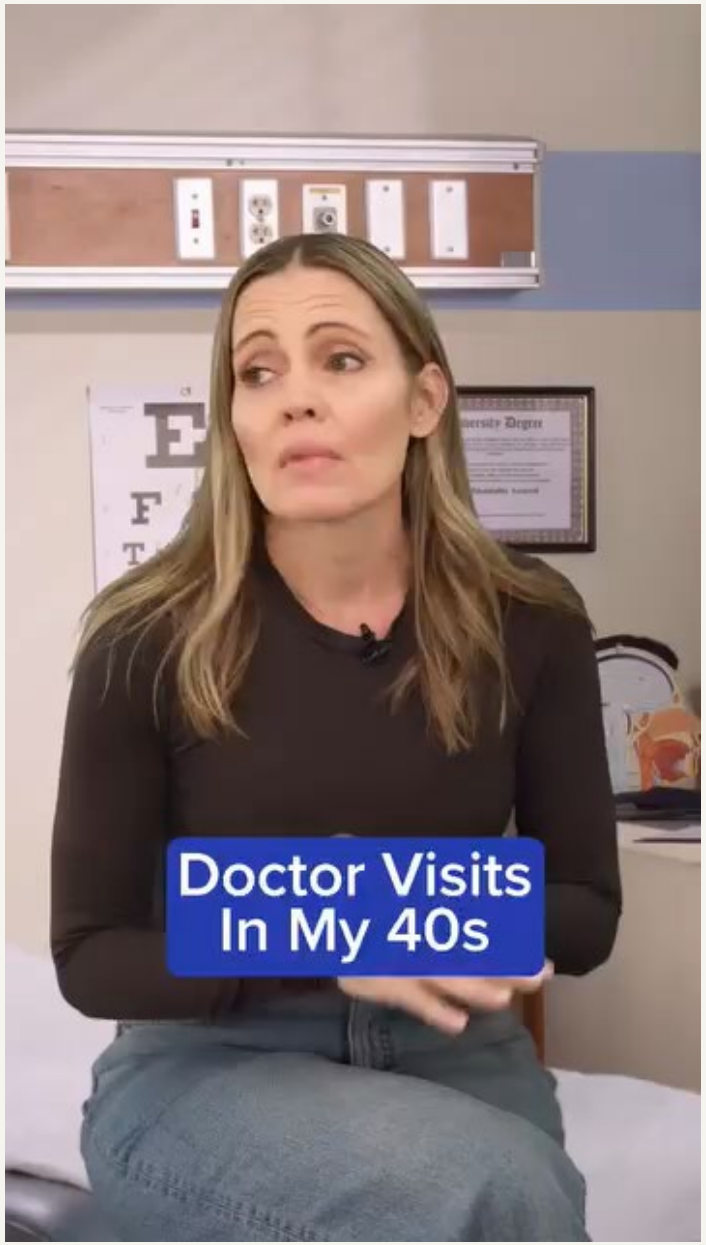
“A full hormone panel reveals what others missed”

“Bioidentical means natural and safer”

“Pellets give stable, optimized levels”



Dr. Mary Claire Haver, MD. There is a lack of education and training around menopause for doctors. Link in description. *YouTube*. Published online June 11, 2025. https://www.youtube.com/watch?v=AfEaIMyEXGI



Holderness K. Doctor visit in my forties. Facebook. https://www.facebook.com/reel/509906191803568



Just Being Melani. Annual Ob/Gyn Appointment. Facebook. https://www.facebook.com/reel/1371029548237650

A POLARIZATION PATHWAY

When marketing reinforces a trust rupture



Real symptoms + prior dismissal

Immediate validation

A villain: “traditional care”

Product as proof of allegiance

Caution becomes “more dismissal”

MAKE THE INVISIBLE WORKLOAD VISIBLE

What arrives in the exam room

12+
supplements

3
hormone tests

1
proprietary “protocol”

∞
saved posts

Do not begin by litigating every item.

- What outcome matters most?
- Which treatment is helping?
- Which item carries the most risk?
- What decision would a lab result change?

A FOUR-STEP RESPONSE

Validate, translate, evaluate, offer



1 VALIDATE **“Thank you for coming to see me about this.”**
“I can definitely help with that!”
“I believe these symptoms are affecting you.”

2 TRANSLATE Convert products and panels back into symptoms, goals, and decisions.

3 EVALUATE Evidence, formulation, dose, reversibility, safety, and financial relationship.

4 OFFER Give an affirmative plan, monitoring strategy, and follow-up.

Visual on this slide was generated with Microsoft Copilot.

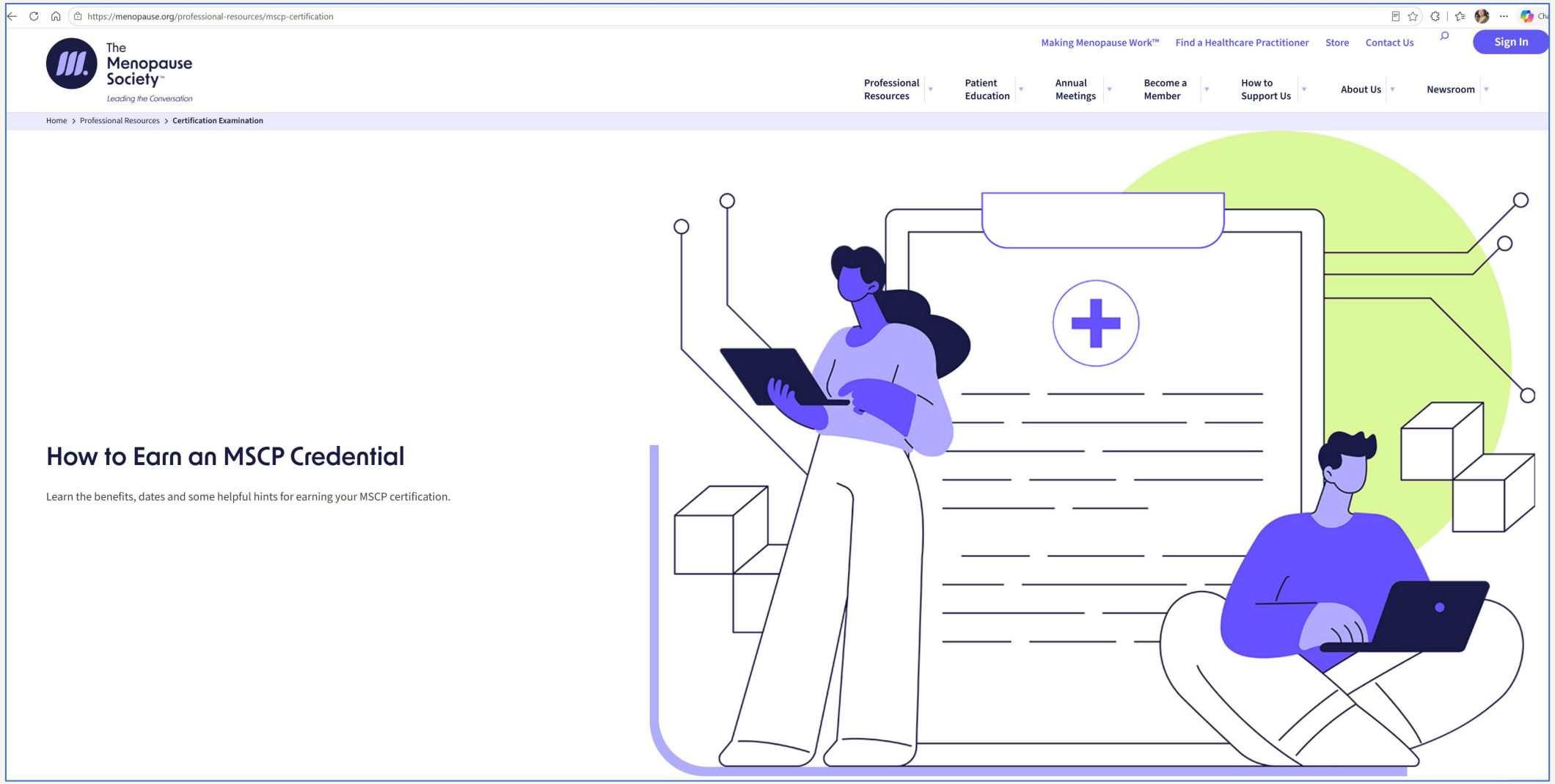
USE AT POINT OF CARE

Ten Guidelines for Practicing Medicine in a Tik-Tok World

1. Menopause and chronologic aging occur concurrently
2. Check labs when the results would change the plan
3. Compounding is an exception
4. We cannot extrapolate low-risk data to high-risk situations
5. We cannot extrapolate low dose data to high dose regimens
6. Effective therapies are published in peer-reviewed journals
7. Incentives do not prove poor care, but failing to disclose a conflict of interest is unethical
8. Commercialization follows unmet need
9. Trust is a clinical intervention
10. Menopause care is primary care

Next Steps

The Next Website I Recommend for You:



Thank you!

