

PRIMARY CARE HAWAI'I CONFERENCE

June 22-26, 2026

Kauai, Hawai'i

GRAND | HYATT
KAUAI RESORT & SPA

20 hours CME Credit

Dr. Katie Massoudian
- No relationships to disclose



Menopause 101

2026 PRIMARY CARE HAWAII CONFERENCE

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CO-LEAD WOMEN'S MIDLIFE WELLNESS
WOMEN'S HEALTH SERVICE LINE
SOUTHERN CALIFORNIA PERMANENTE MEDICAL GROUP
CLINICAL FACULTY - BERNARD TYSON SCHOOL OF MEDICINE



Menopause Myths

- PERIODS AND PMS PEACEFULLY RIDE INTO THE SUNSET
- PERI/MENOPAUSE SYMPTOMS CAN'T BE TREATED UNTIL ONE YEAR WITHOUT A PERIOD
- WOMEN SHOULD “MUSCLE” THROUGH HOT FLASHES
- MHT (HRT) IS ALL YOU NEED

Menopause Transition

“THIS IS BOTH A WINDOW OF VULNERABILITY AND WINDOW OF OPPORTUNITY”

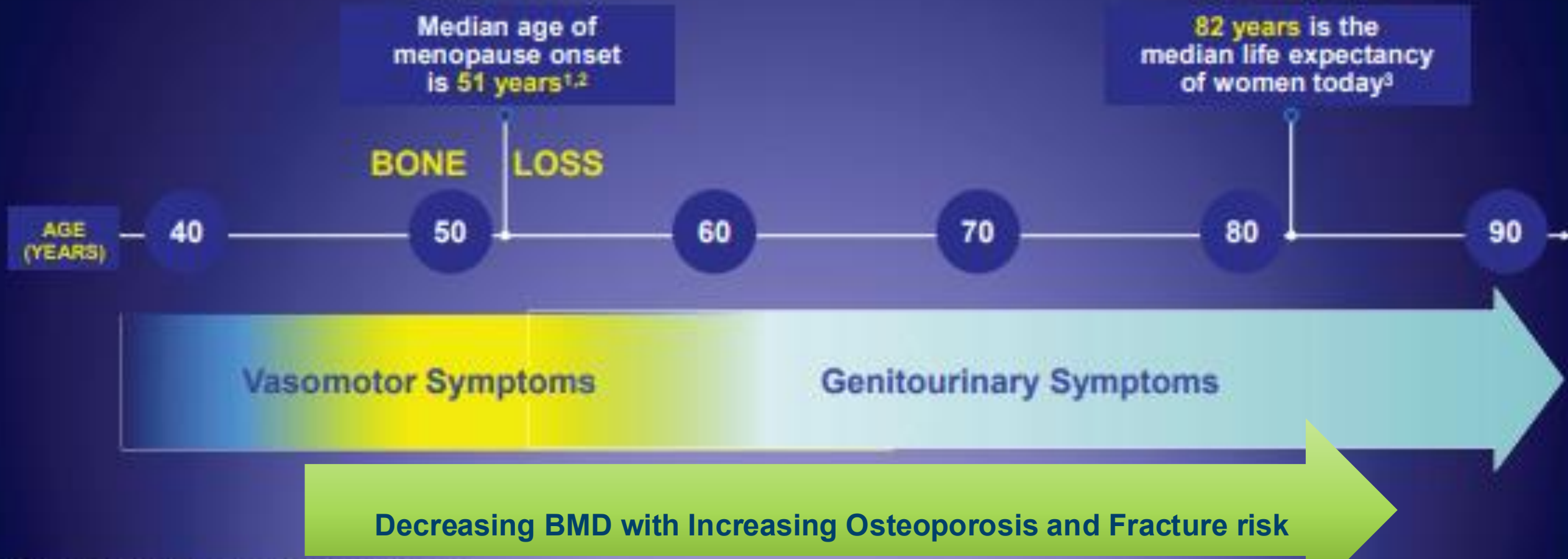
- Transition marks beginning of increased risk for CVD, DM, Osteoporosis and cognitive decline
- Valuable cue for women to invest in lifestyle changes that pay dividends in later years through nutrition, physical activity, mindfulness, and community building



AN
Oprah
 SPECIAL
 The
Menopaus
 Revolution



Women are Menopausal More Than One-third of Their Lives



1. Parish SJ, et al. *Menopause*. 2018;25(8):937-941

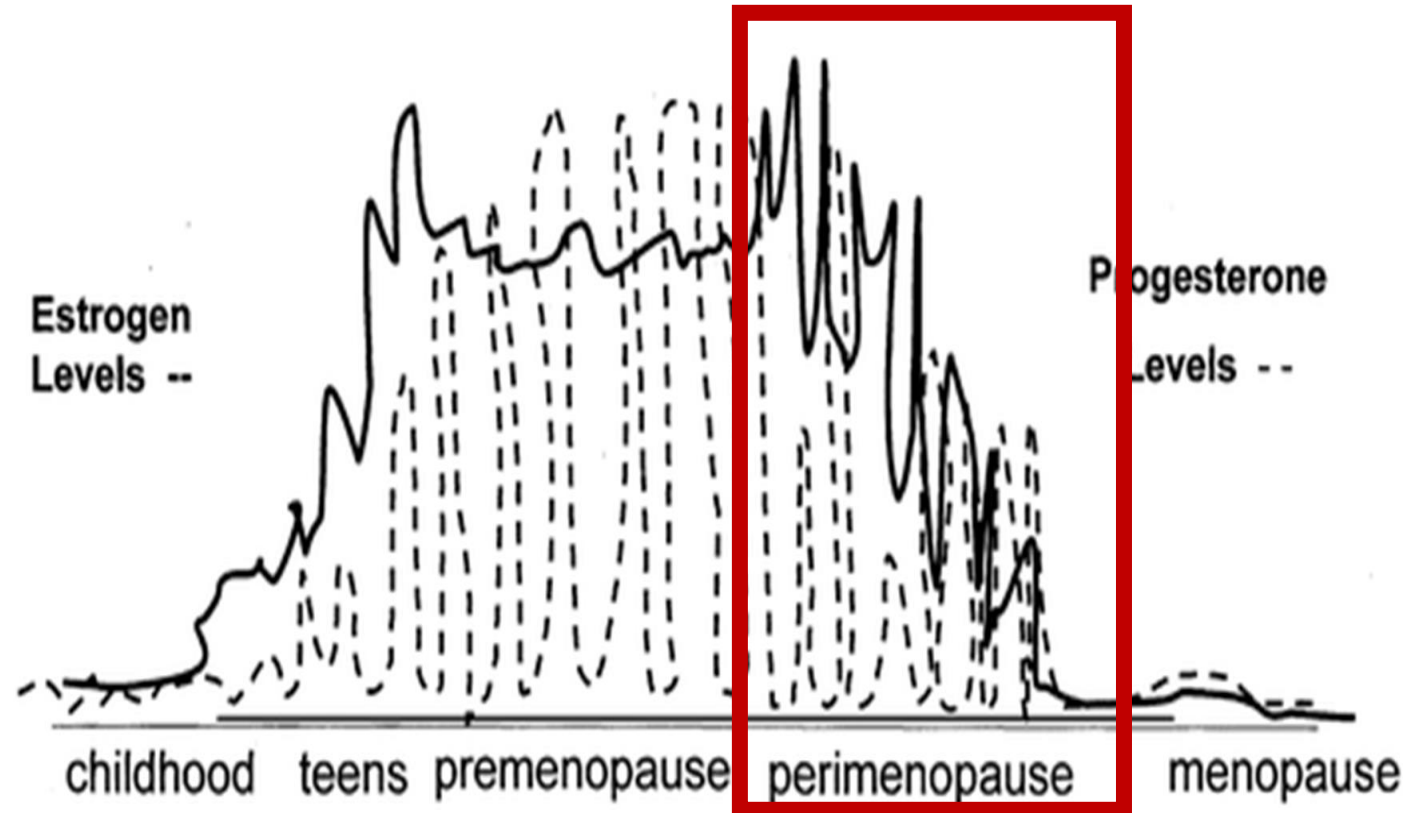
2. North American Menopause Society. *Menopause 101*. www.menopause.org/forwomen/menopause/flasher/menopause-symptoms-and-treatment/menopause-101-a-primer-for-the-perimenopausal. Accessed March 25, 2019.

3. US Census Bureau. www.census.gov/data/tables/2014/totalpop/totals.html#t01

Definitions and Statistics:

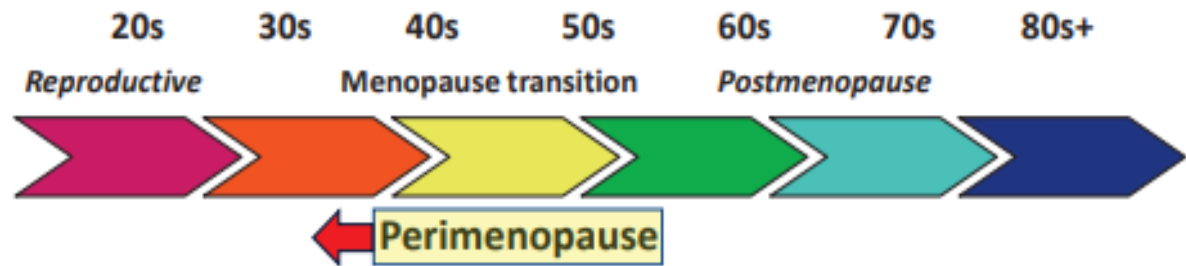
- Menopause: 12 months of amenorrhea due to ovarian follicular depletion
- Average onset: 51 years; transition lasts 4–10 years
- Marked decline in estradiol, progesterone; rise in FSH/LH
- Systemic consequences across nearly every body system
- **Early menopause**(ages 40-45) varies 2.9 – 4.1% based
- **Premature Ovarian Insufficiency** (at under age 40) occurs in 1% of women

Life Cycles of Ovarian Hormones



SWAN Data

The Perimenopause “...not feeling like myself”



Includes the years prior to menopause when **menstrual cycles change** and one year after the final menstrual period



Symptoms:

Hot flashes and brain fog
Altered mood and sleep
Genitourinary syndrome
Bone loss begins

Harlow SD, et al. *Menopause* 2012;19:387-95; Santoro N, et al. *J Clin Endocrinol Metab* 2021;106:1-15.



Proportion of women in each ethnic group in the SWAN longitudinal study (n=3,302).



Menopause Experience: Racial and Ethnic Differences

- Peak incidence of VMS during late perimenopause (~age 49 episodes \geq 2 months amenorrhea)

| | DURATION |
|---------------------|----------|
| Black women | 10 y |
| Non-Hispanic white | 9 y |
| Chinese or Hispanic | 5 y |

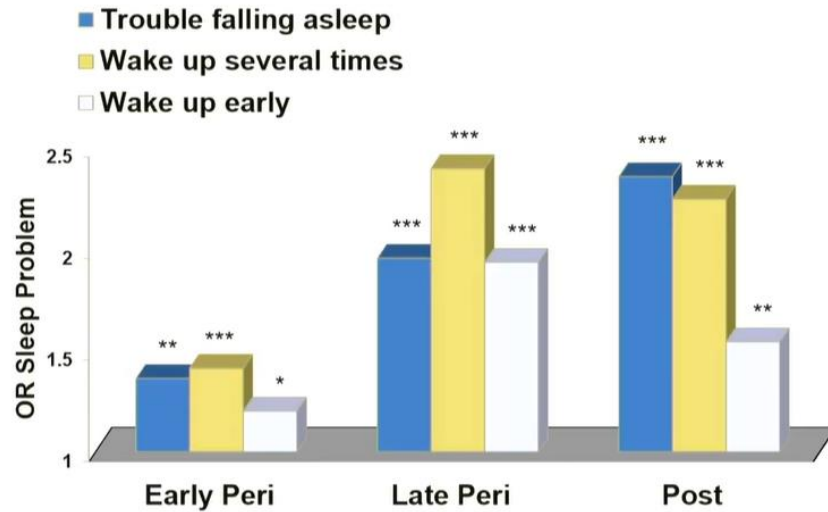
- Factors with increased VMS frequency
 - Black and White race
 - BMI > 30 1.5-fold
 - Smoking > 40 pack-yr 2.0-fold

Crandall CJ, *JAMA*, 2023 Feb 7



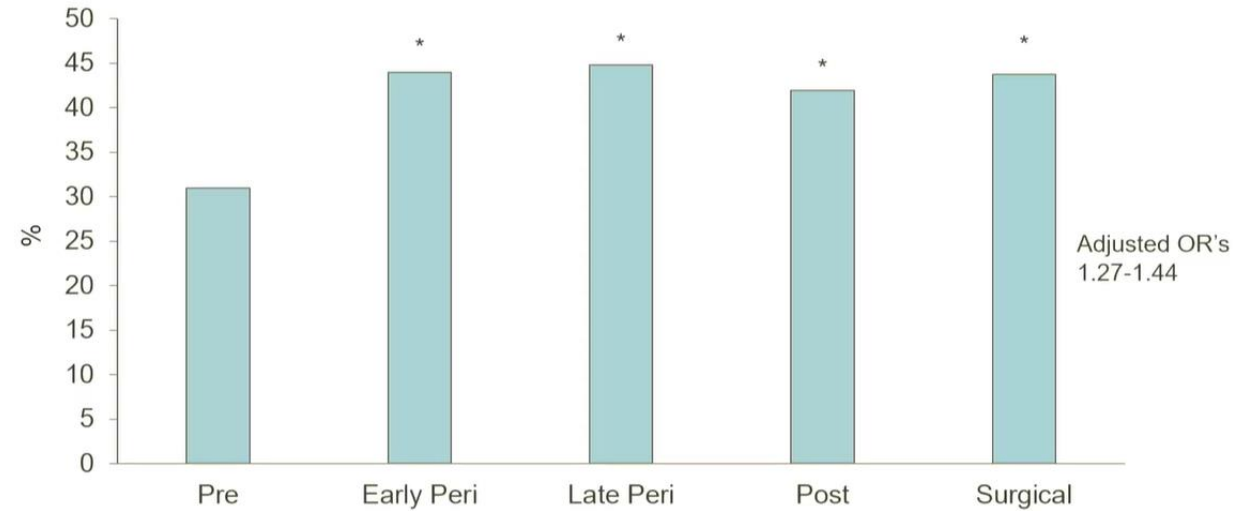
SWAN: SLEEP PROBLEMS WITH THE MENOPAUSE TRANSITION

(Kravitz et al., 2008, *Sleep*)



*p<0.05, **p<0.01, ***p<0.001 vs. premenopausal
Adjusted for age, race, site, vasomotor sx, E2, FSH, N=3045

SWAN: REPORTS OF FORGETFULNESS BY MENOPAUSE STAGE



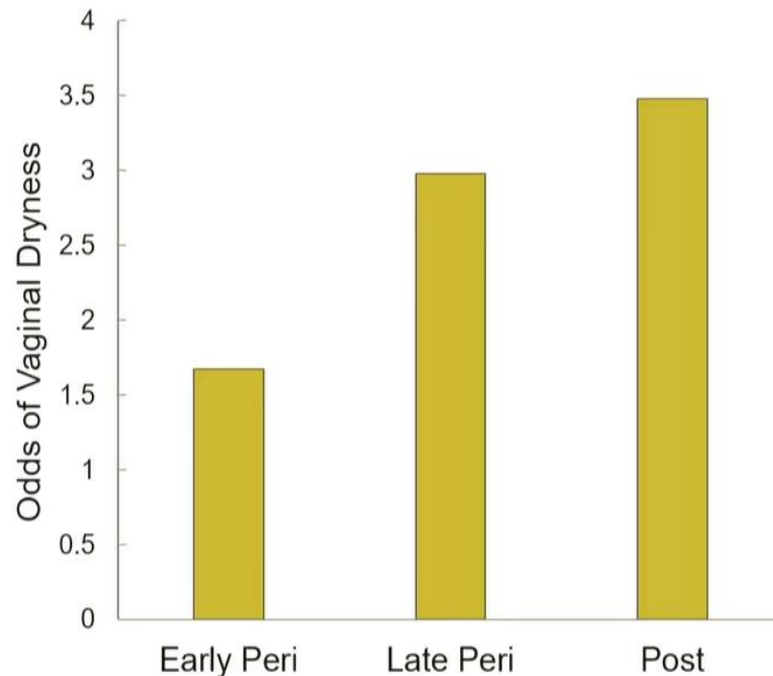
*p<.05, relative to pre, multivariable

Adjusted OR's
1.27-1.44

(Gold et al., 2000, *Am J Epidemiol*)

VAGINAL DRYNESS

(Waitjen, 2018, *Menopause*)



43% of US midlife women ages 55-65 report vaginal discomfort
(Nappi, 2010, *Maturitas*)

NOT FEELING LIKE ONESELF

(Coslov et al., *Menopause*, 2024)

- Survey of 1263 women ages 35-55
- 63% reported “not feeling like themselves”



Early Perimenopause

- Increased PMS
- Insomnia
- Memory problems
- Increased anxiety and depression
- Subtle changes in cycles



Late Perimenopause

- Early perimenopause symptoms AND
- Hot flushes symptoms likely
- Vaginal dryness likely
- 2 or more skipped cycles and greater than 60 days amenorrhea



Early Postmenopause

4years

- Begins at 12 months of amenorrhea
- Increased hot flushes
- Increased night sweats
- Increased vaginal dryness
- Increased sleep disturbances



Late Postmenopause

- GSM
- Incontinence
- Osteoporosis
- CVD
- Vasomotor symptoms can linger

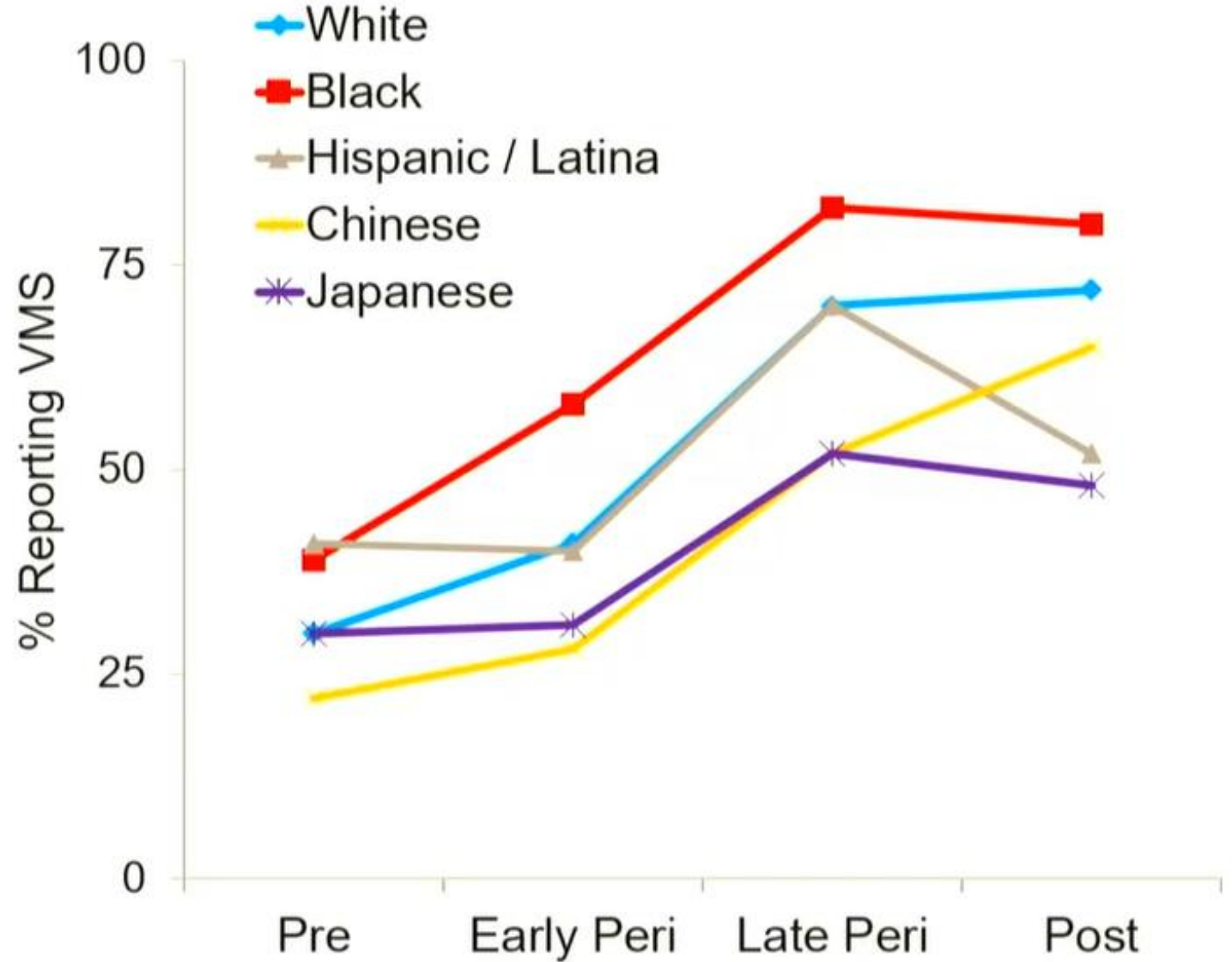
Onset 40-50's

Until Demise



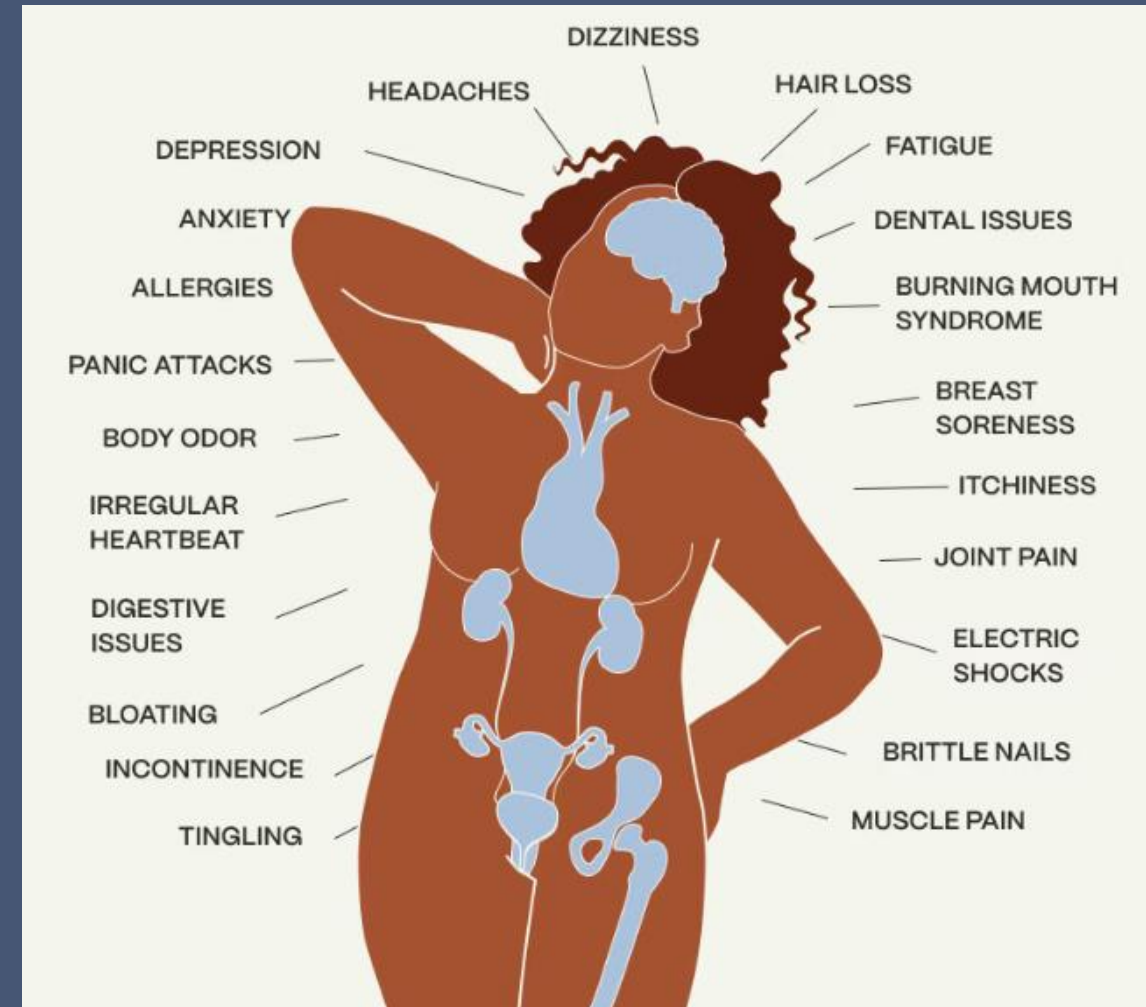
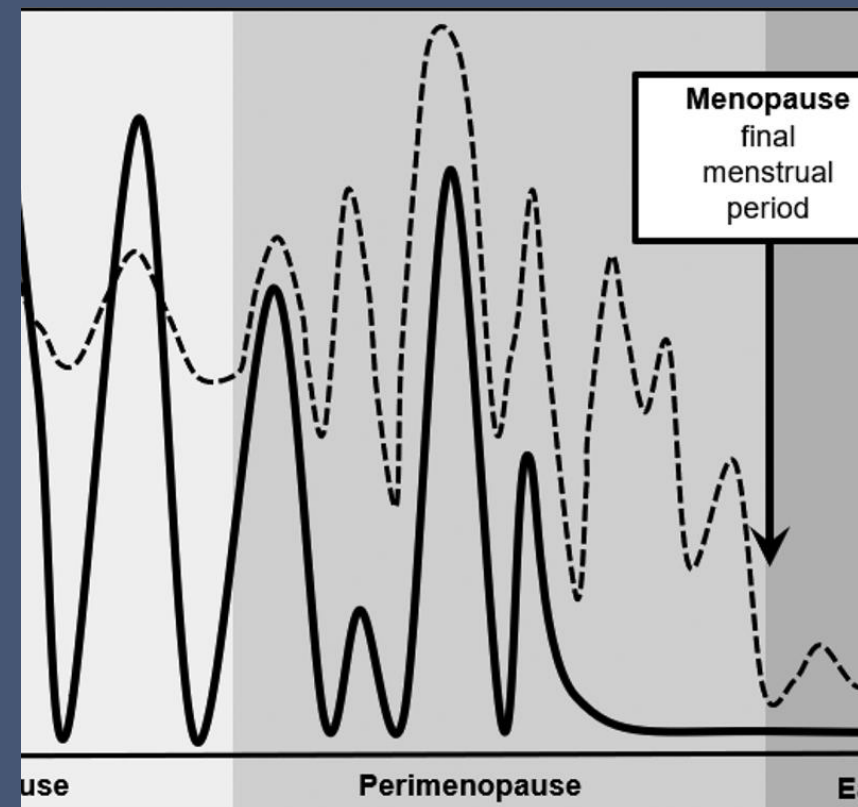
SWAN: VASOMOTOR SYMPTOMS (VMS) OVER THE MENOPAUSE TRANSITION

(Gold et al., 2006, *AJPH*)

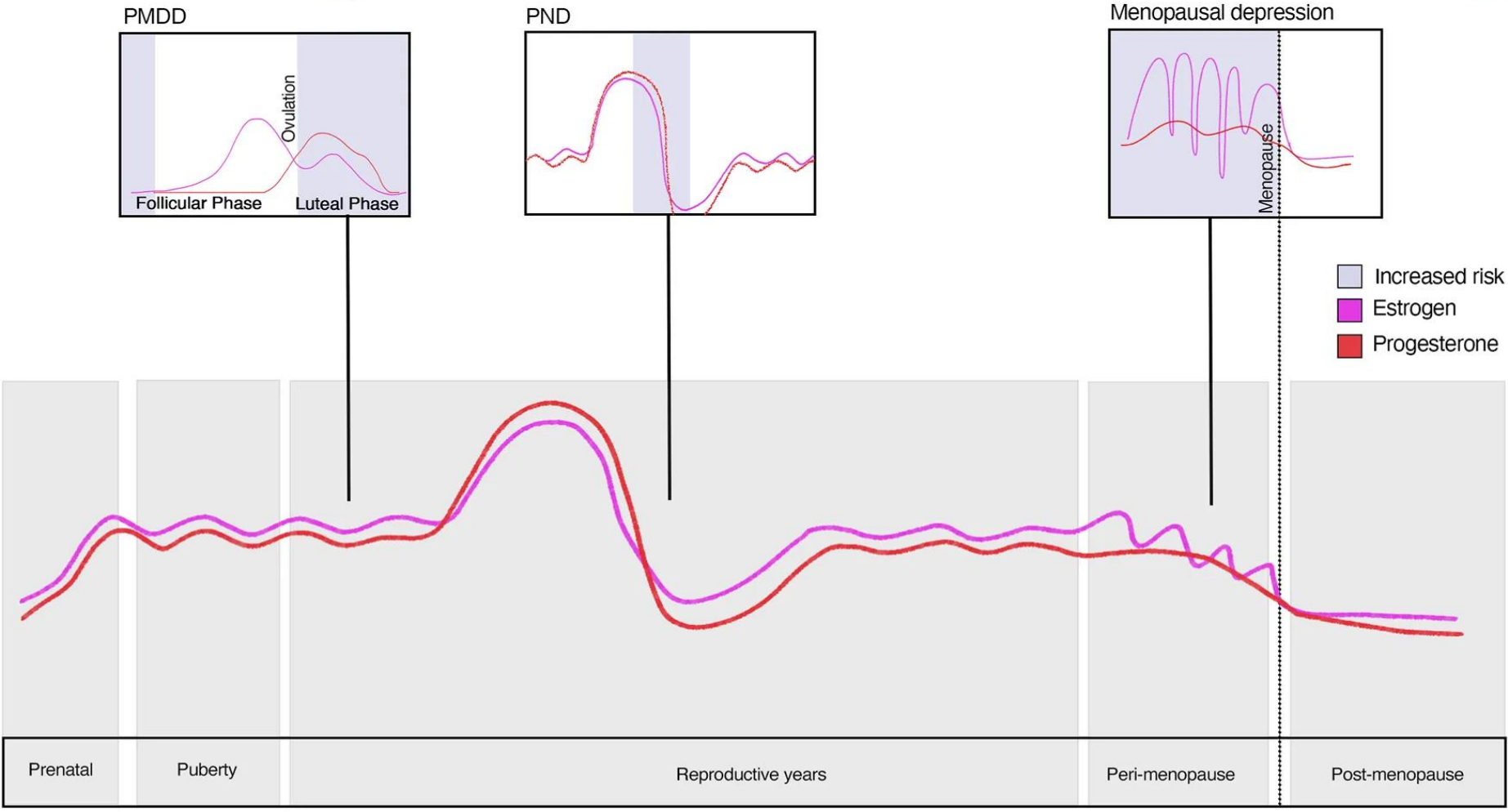


PERIMENOPAUSE – INCONSISTENTLY CHAOTIC

- **HORMONE FLUCTUATIONS** are hallmark
- **Menstrual Chaos** is common
- Rely on recent HPI and Symptom timing



Perimenopausal Mood Fluctuation



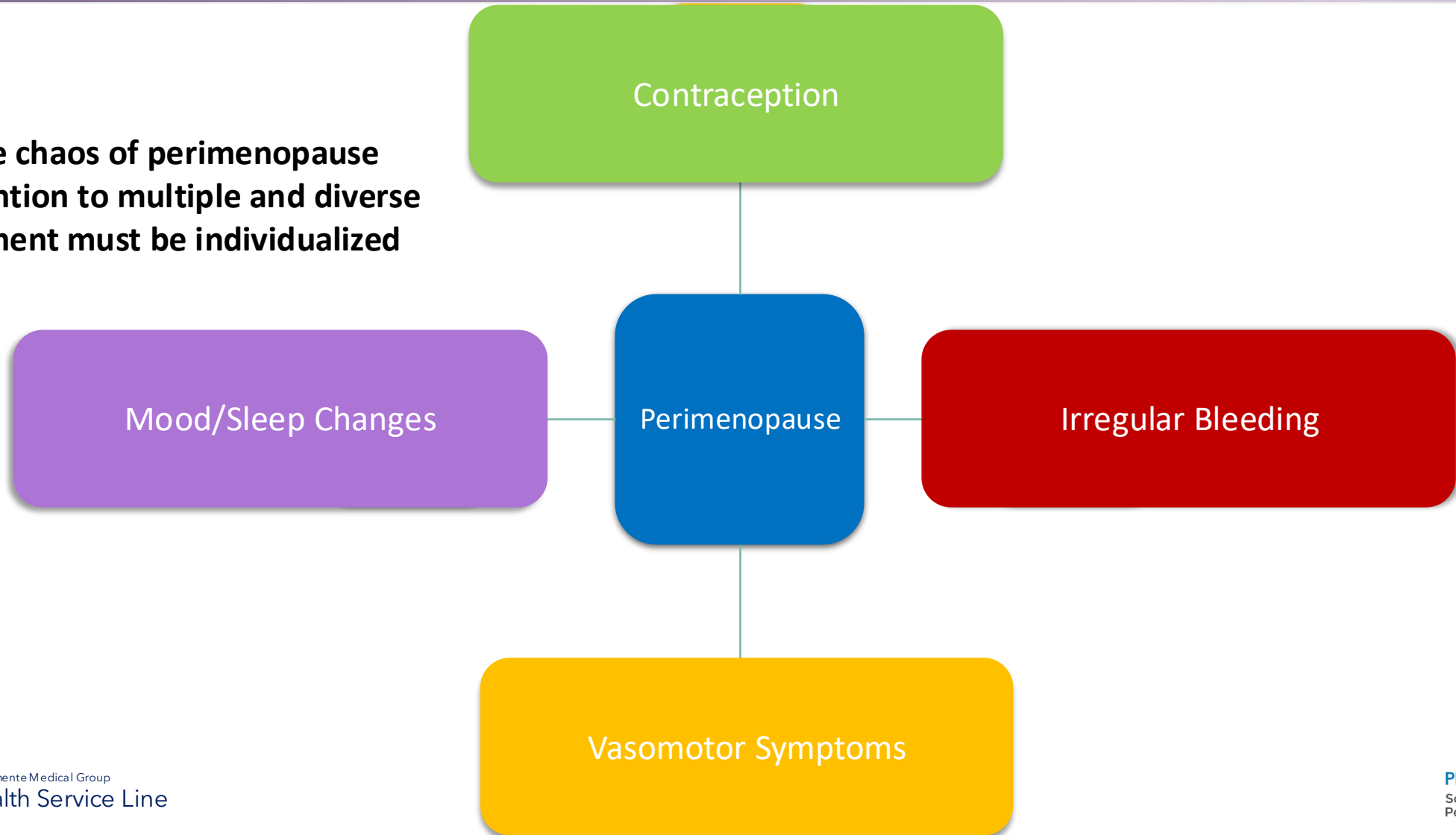
Risk Factors

1. PMS/PMDD
2. Perinatal Depression
3. Existing GAD or MDD
4. VMS
5. Insomnia
6. SDH



Managing Perimenopause: More than Symptom Control

Managing the chaos of perimenopause requires attention to multiple and diverse issues: treatment must be individualized



HOT FLASHES- benign waves of warmth?

Hot flashes are associated with declines in memory and adverse effects on the brain

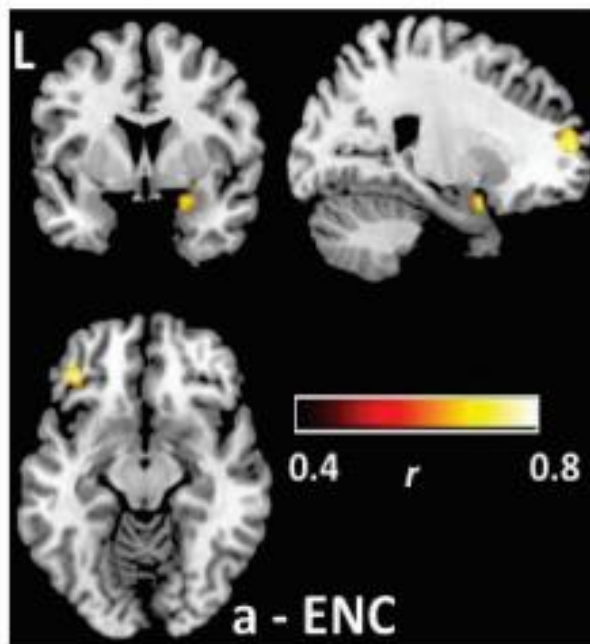
Decreased Verbal Memory



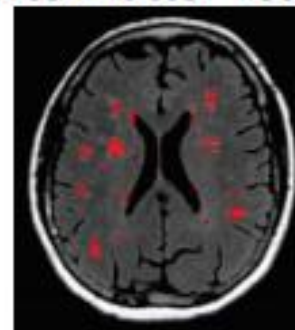
Alzheimer's Disease Biomarkers



Altered Activity in Brain Circuits as Women Learn Words



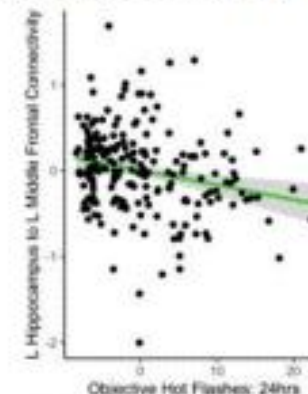
White Matter Lesions



Decreased Hippocampal Functional Connectivity



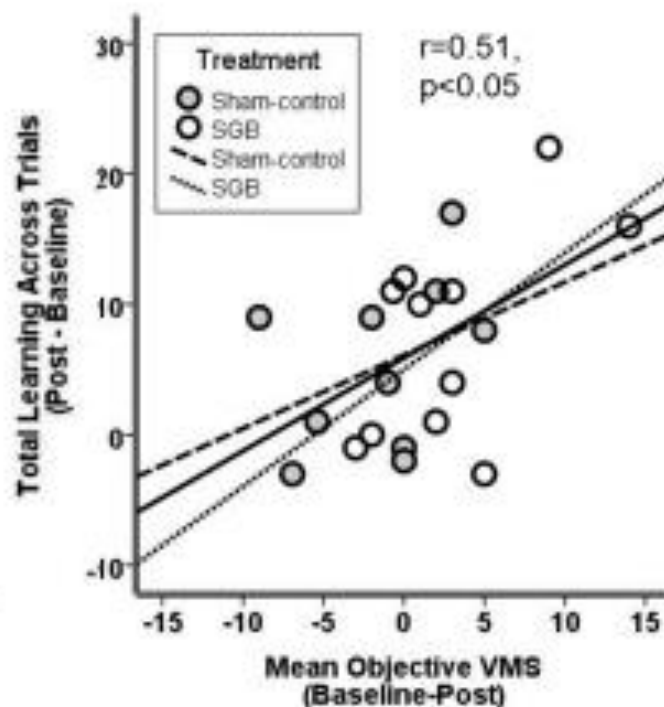
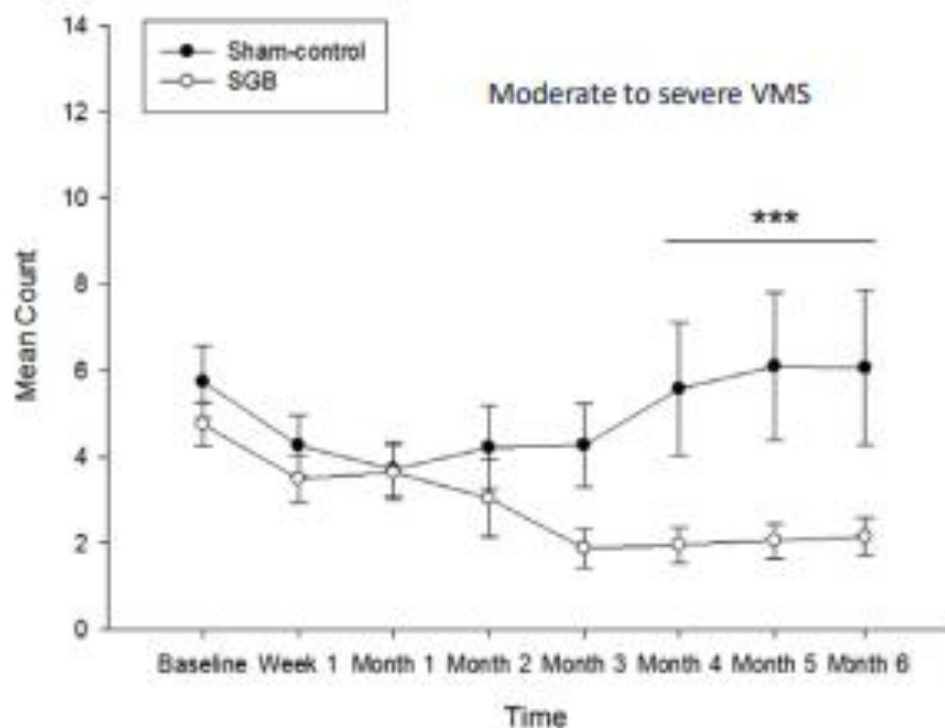
- L Hippocampus Seed
- L Middle Frontal Gyrus
- L Superior Frontal Gyrus



Maki PM et al. Objective hot flashes are negatively related to verbal memory performance in midlife women. *Menopause*. 2008;15(5):848-856; Fogel J., Maki PM. Physiologic vasomotor symptoms are associated with verbal memory dysfunction in breast cancer survivors. *Menopause*. 2020 Nov 1;27(11):1209-18; Maki PM et al. Stellate ganglion blockade and verbal memory in midlife women: Evidence from a randomized trial. *Maturitas*. 2016 Oct 31;92:123-9; Thurston RC, Maki PM, et al. (2015). Menopausal hot flashes and the default mode network. *Fertility and Sterility*. Thurston . Maki, *Neurology*, 2022



Initial evidence that VMS treatments might improve memory in women with moderate-to-severe VMS



Decreases in physiologic VMS correlate with improvements in verbal memory in a clinical trial of stellate ganglion blockade

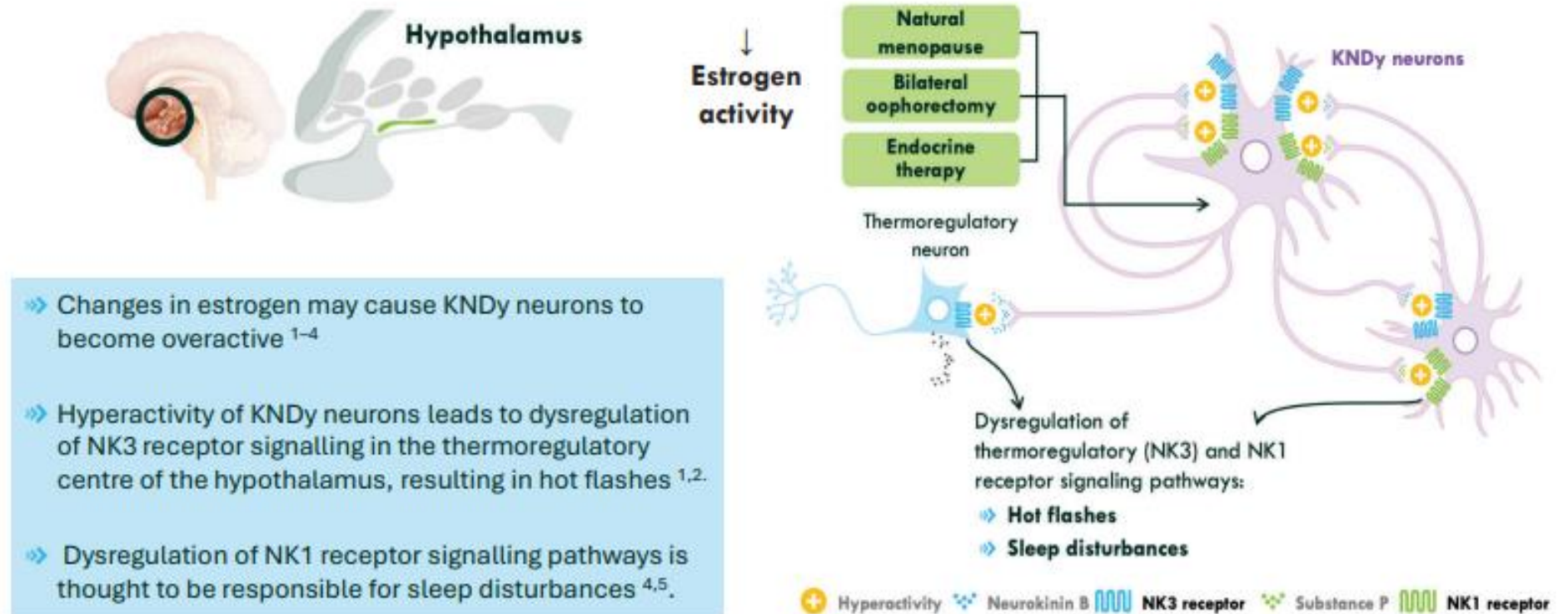
Walega DR, Rubin LH, Banuvar S, Shulman LP, Maki PM. Effects of stellate ganglion block on vasomotor symptoms: findings from a randomized controlled clinical trial in postmenopausal women. *Menopause*. Aug 2014;21(8):807-814.

Maki PM, Rubin LH, Savarese A, Drogos L, Shulman LP, Banuvar S, Walega DR. Stellate ganglion blockade and verbal memory in midlife women: Evidence from a randomized trial. *Maturitas*. 2016 Oct 31;92:123-9.



- Changes in Estrogen may cause hyperactivity of KNDy neurons
- Hyperactive KNDy neurons -> dysregulation of thermoregulatory NK3 receptors -> hot flashes
- NK1 receptor dysregulation thought to lead to sleep disturbances

KNDy neurons, thermoregulation, and sleep



KNDy, kisspeptin/neurokinin B/dynorphin; NK, neurokinin.

1. Cardoso F, et al. *N Engl J Med* 2025;393:753–63; 2. Pinkerton JV, et al. *JAMA* 2024;332:1343–54; 3. Rance NE, et al. *Front Neuroendocrinol* 2013;34:211–27; 4. Simon JA, et al. *Menopause* 2023;30:239–46; 5. Sergeeva OA, et al. *Peptides* 2022;150:170729.

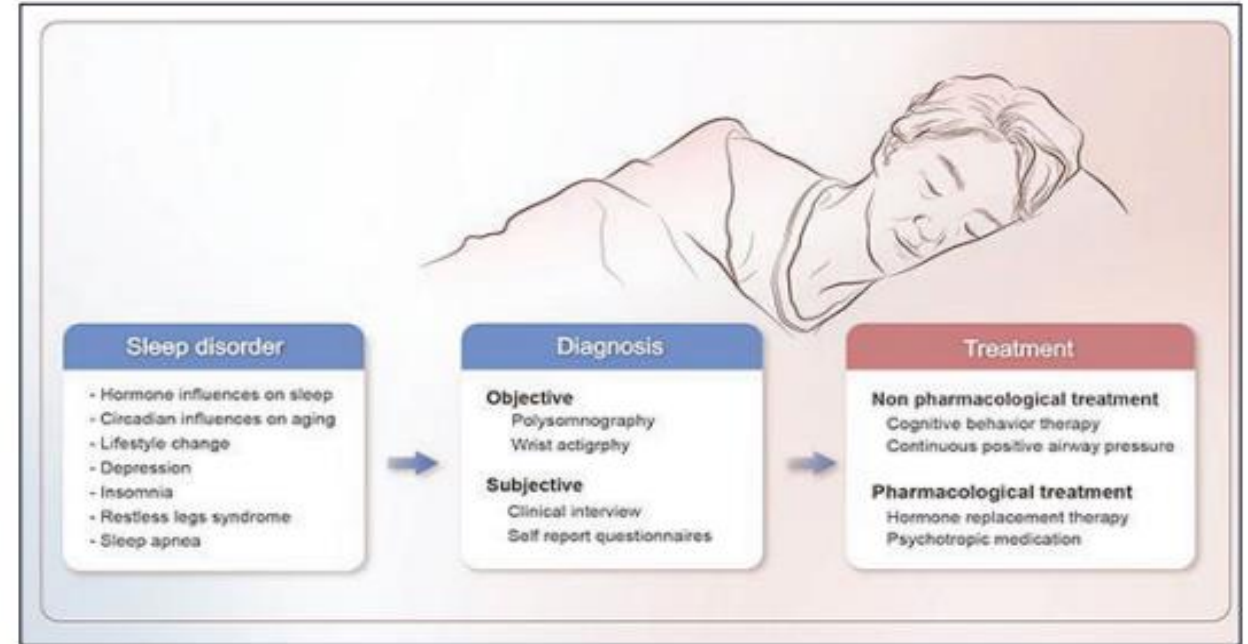
Fezolinetant (NK3) and Elinzanetant (NK3 + NK1)



Sleep Disorders in Midlife

- Inadequate sleep:
 - Sleep duration >9 or <7 hours
 - Poor sleep quality
- Decreased sleep duration during MT
- Increased incidence of obstructive sleep apnea
 - Severe VMS linked to OSA
- Associated **↑** with obesity, insulin resistance, HTN and worse CVD outcomes

Dastmalchi, et al. JACC Adv. 2025



Han, et al. J Menopausal Medicine. 2019



'EARLY' PERIMENOPAUSE



Hormones*

↔ E₂ (relatively unchanged)

↑ FSH *

CVD Risk Factors

↑ C-IMT and vascular remodeling

↓ Endothelial function (FMD)

NOTE: Few studies of women in *early perimenopause* have been conducted due to the inherent difficulty in categorizing women in this earlier stage. As a result, the cardiometabolic changes that occur during *early perimenopause* have yet to be fully elucidated.

'LATE' PERIMENOPAUSE



Hormones*

↓ E₂ * and AMH

↑ FSH *

Body Composition

↑ Fat mass (abdominal fat)

↓ Fat-free (lean) mass

Energy Intake & Expenditure



↓ 24-h, Sleep, & Physical Activity EE
Resting EE (?)
Fat oxidation
Energy Intake

Cardiovascular Risk Factors



↑ Dyslipidemia
(mostly within 1-year of FMP)
↑ C-IMT, Aortic PWV, and
vascular remodeling
↓ Endothelial function (FMD)
and cardiac health
↑ Insulin resistance
↑ Sleep disturbances

POSTMENOPAUSE

Hormones*

↓ E₂ (for 2 years after FMP, then stabilizes) *

↑ FSH (for 2 years after FMP, then stabilizes) *

Body Composition

↑ Fat mass (abdominal fat)
(for 2 years after FMP, then stabilizes)

↓ Fat-free (lean) mass
(for 2 years after FMP, then stabilizes)

Energy Intake & Expenditure

↓ 24-h and Sleep EE
Physical Activity EE
Fat oxidation
(remains low into postmenopausal years)

Cardiovascular Risk Factors

↑ Dyslipidemia
(mostly within 1-year of FMP)
↑ Insulin resistance and glucose intolerance
(associated with abdominal fat accumulation)
↑ Sleep disturbances

Key Considerations in Midlife



Midlife is a crucial window for implementing early prevention strategies to reduce future CVD risk



Emphasis should be placed on lifestyle modifications including a healthy diet, regular exercise, weight management, and avoiding smoking



Awareness of Female Specific risk factors and modification is important—migraine, depression, autoimmune diseases, adverse pregnancy outcomes



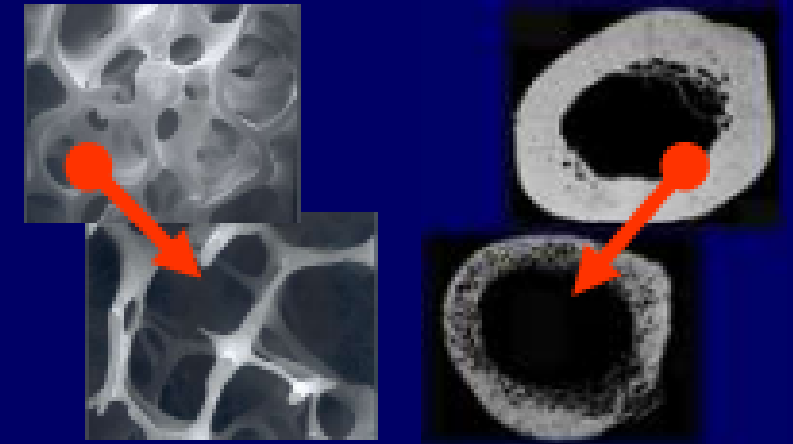
Expanding CVD risk assessments to include the impact of social determinants of health and nonbiological factors to address health disparities



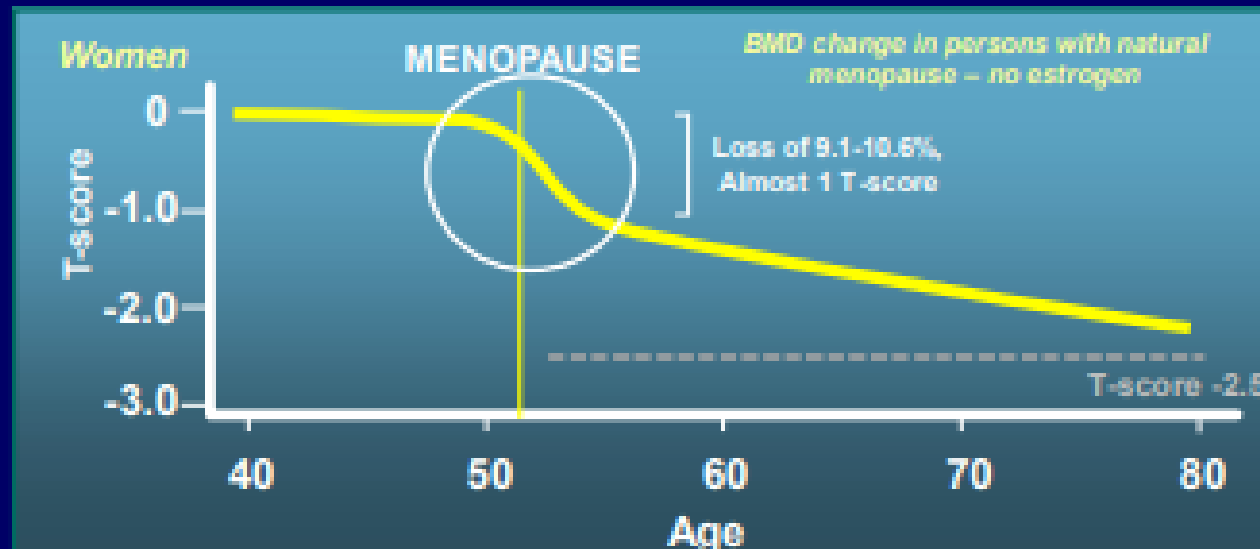
Menopausal Transition: Rapid Bone Loss

Key Points:

- Bone loss is a continuous process beginning during perimenopause. Relatively rapid loss occurs from ~2 years before until several years after the FMP
- Transmenopausal bone loss is as a key factor contributing to the subsequent development of osteoporosis



Images Courtesy of Drs. David Dempster and Roger Zebazi



Study of Women Across the Nation (SWAN)
3302 pre- or peri-menopausal women ages 42 - 52 years have been followed across the menopausal transition

BMD measured in 2407 women at 5 study sites

Data adapted from SWAN and NHANES studies
Greendale GA et al. *J Bone Miner Res* 2012;27:111-8
Looker AC et al. *NCHS Data Brief* 2012;93:1-8

Bone Health – Preventing Osteoporosis

- Bone density decrease starts around early 40's and accelerates 2-3 year before menopause
- Lifestyle factors influencing bone: smoking, weight, diet, genetics
- Why important? A woman's risk of dying from a hip fracture **exceeds** that of breast cancer, uterine cancer, and ovarian cancer combined.
- Prevention is the best intervention
 - Strength training/vit D/Ca⁺⁺/TOBACCO CESSATION
 - Bisphosphonates
 - SERMS: Raloxifene, Bazodoxifene
 - Estrogens



NAMS 2022: Genitourinary Syndrome of Menopause (GSM)

- The most inevitable, prevalent and progressive change seen with menopause

Symptoms

- Irritation, burning, or itching of the vulva or vagina
- Urinary frequency, urgency, dysuria

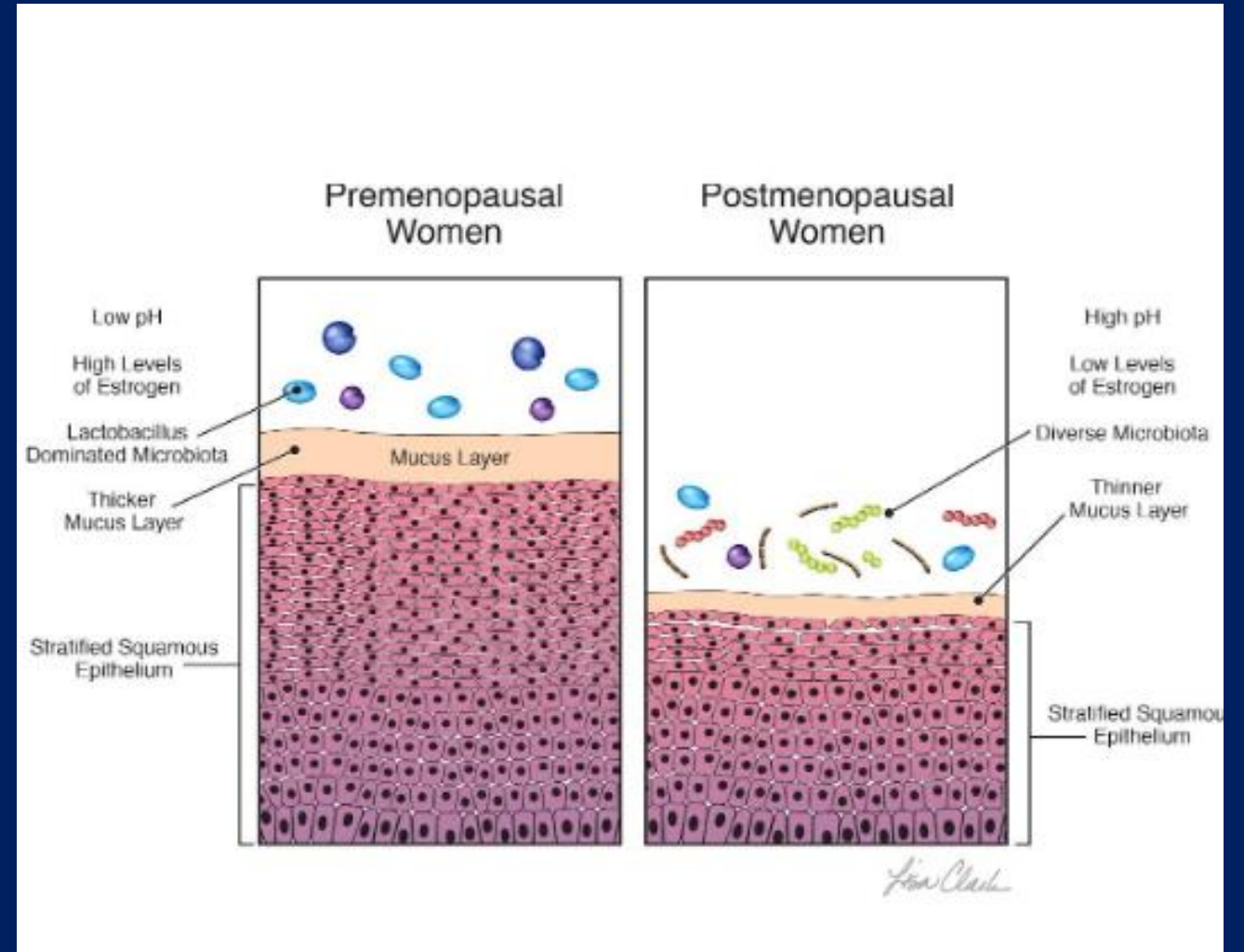
Signs

- Tissue fragility, fissures, petechiae
- Urethral eversion or prolapse

Treatment

- Low dose vaginal estrogen therapies are effective and generally safe for treatment of GSM with minimal systemic absorption
- For women with breast cancer, low-dose ET should be prescribed in consultation with oncologists
- More concern for those on aromatase inhibitors
- Progestin therapy not required for low-dose vaginal therapy but data not likely available beyond 1 year


North American Menopause Society. Menopause. 2022;29(7):767-94.







Genitourinary Syndrome of Menopause: Vaginal Estrogen and Recurrent UTI


2022: 10 year MCRT incl. 5,638 women,
age ≥ 18 (Mean age: 70.4)


 Diagnosed with recurrent UTI (≥ 3
UTIs/year)

 Prescribed vaginal estrogen

 Includes menopause, oophorectomy,
breastfeeding, etc.


 Pre-treatment: 3.9 UTIs/year


 Post-treatment: 1.8 UTIs/year (\downarrow
51.9%)

 55.3% had ≤ 1 UTI in 12 months


 31.4% had 0 UTIs post-treatment

Higher adherence linked to lower UTI
recurrence

 Clear trend between estrogen use and
outcome improvement

 Vaginal estrogen use significantly
reduces recurrent UTIs in hypoestrogenic
women

 Supports its role in prevention
strategies

 Encourage adherence for optimal
outcomes

[Tan-Kim, et al, AJOG 2023](#)

GSM: Vaginal Estrogen & Recurrent UTI & Urosepsis

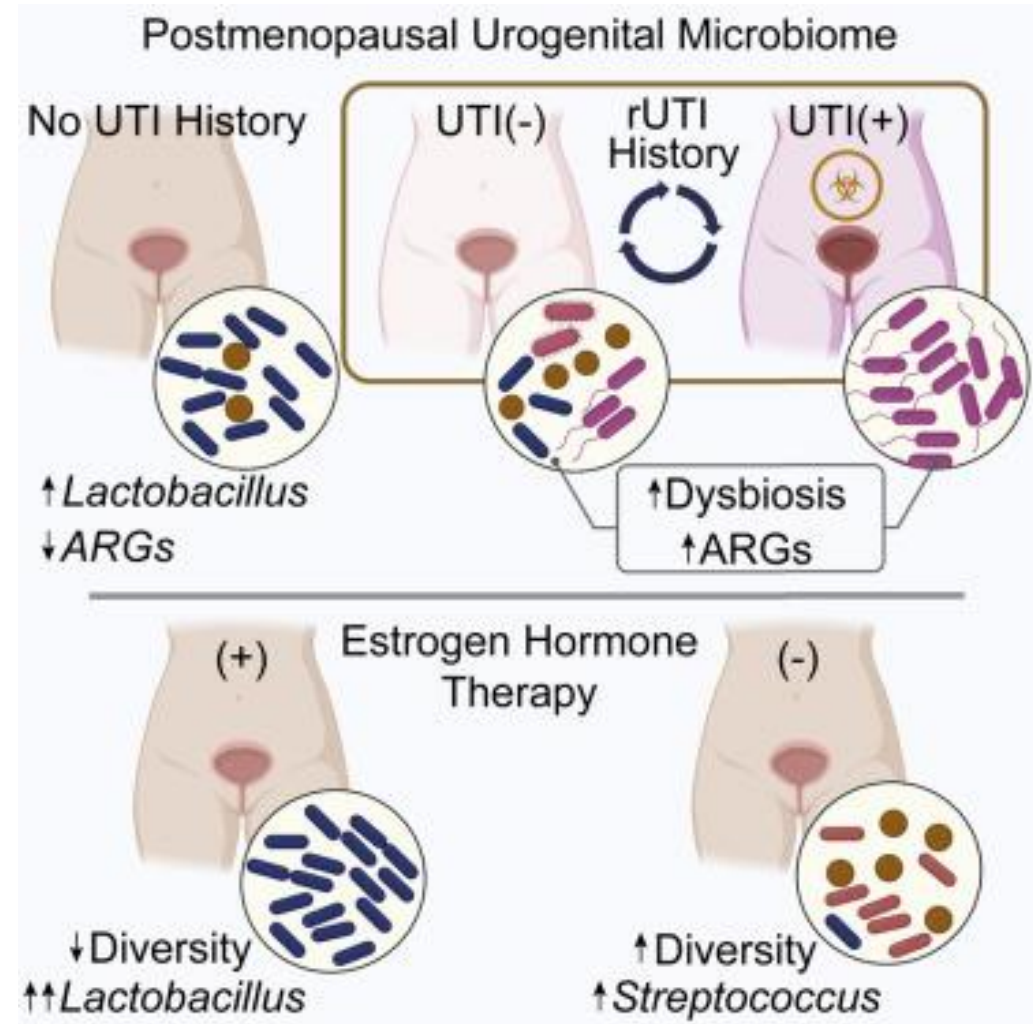
[2025 Presentation at AUA \(Urology\) Annual Meeting:](#)

Study Population: Data from **2,163,216 female patients** with recurrent urinary tract infections (UTIs) were analyzed using Epic EHR systems over a 3-year period.

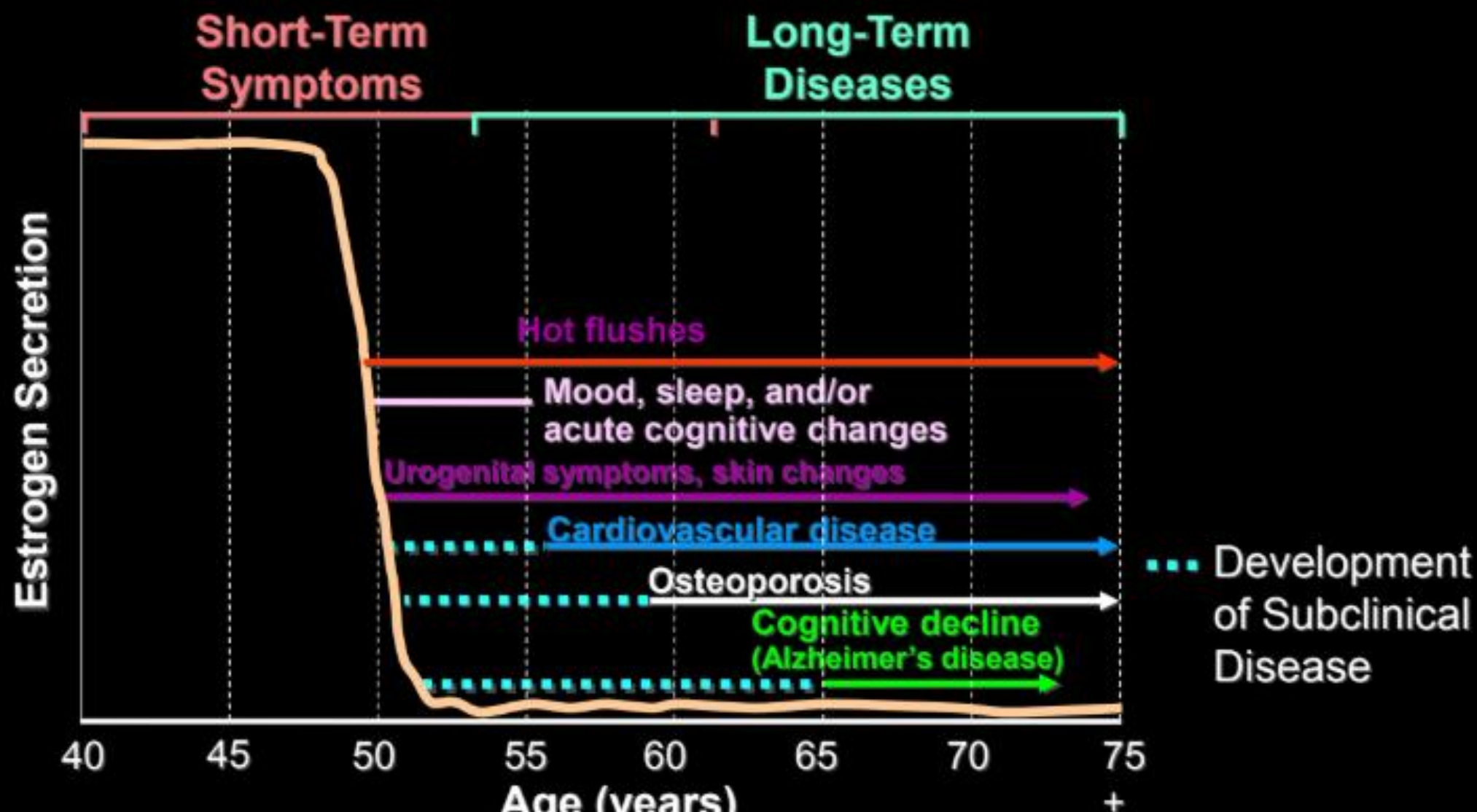
Comparison Groups: Patients using vaginal estrogen were compared to those not using it, focusing on adverse outcomes: sepsis, hospital admissions, and mortality.

Key Findings (Postmenopausal Women):

Women over 55 using vaginal estrogen had **significantly lower** rates of **sepsis (10.6% vs 19.4%), hospitalization, and death (0.42% vs 1.54%)** compared to non-users



Estrogen Loss and Manifestations of Health Risks Over Time



What About the WHI?

PERMANENTE MEDICINE®

Southern California
Permanente Medical Group

- RCT 1993-2002, ~\$1B
- 27000 US women 50-79yo
- Primary endpoint – HT in Primary prevention of Heart Disease
- **Mean age 63yo**
- Two treatment arms
 - Oral CEE + MPA (*Prempro*) vs Placebo (uterus)
 - Oral CEE alone vs Placebo (no uterus)
- Multiple sub-analyses and reconsiderations in past 15 years
- At start of trial 40% of US women on HT; today 6-8% of eligible US women on MHT



WHI Primary Investigator,
Endocrinologist Joanne Manson:

“The WHI findings have been seriously misunderstood and misinterpreted.”

August 2016

New York Times [editorial](#) 2016

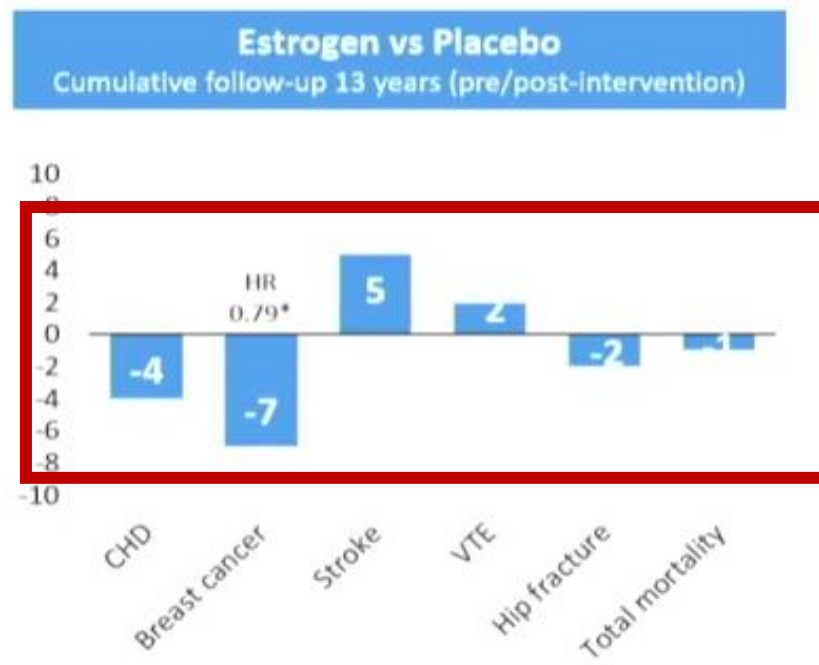
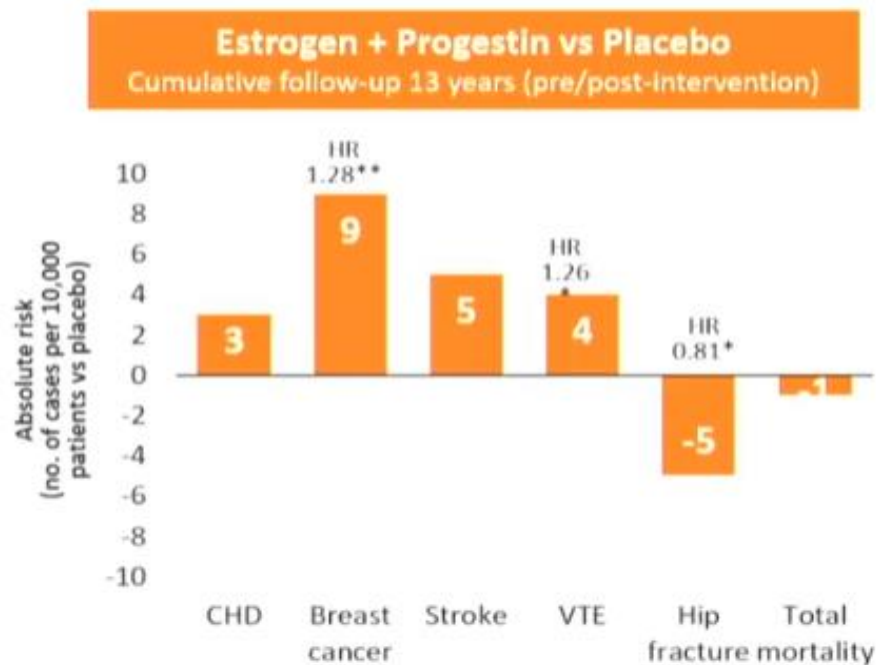
Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal Hormone Therapy and Health Outcomes During the Intervention and Extended Poststopping Phases of the Women's Health Initiative Randomized Trials. *JAMA*. 2013

Long-term Follow-up for EPT Trial: Post-intervention Analysis

WHI

CEE + MPA and CEE alone

CEE = conjugated equine
Estrogen



DECREASED breast cancer, CHD, fracture, and all cause mortality in the estrogen only group

Hazard ratios (HR) shown represent relative risk vs placebo.

*P<0.05; **P<0.001.

CEE, conjugated equine estrogen; CHD, coronary heart disease; HR, hazard ratio; VTE, venous thromboembolism

Manson JE et al. *JAMA*. 2013;310(13):1353-8.



A hard lesson learned

As data from RCTs accumulate, the results look more and more like the 20+ consistent observational studies that indicate that young, symptomatic postmenopausal women who use HRT for long periods of time have lower rates of CHD and total mortality than postmenopausal women who do not use HRT, with rare risks that are comparable to or lower than other commonly used medications and supplements.

Hodis et al, *Climacteric* 2012;15:217-228



Best Evidence: Benefits of MHT Outweigh Risks for Most Newly Menopausal Women

- Why consider MHT?^{1,2}
 - Menopausal symptoms are commonly experienced by women
 - MHT is currently the standard of care for VMS and GSM
 - MHT demonstrated benefits for bone protection and joint pain
 - MHT may improve mood disorders, sleep, sexuality, and quality of life
- So what are the lingering issues?
 - 60-70% of women discontinue MHT before 1 year^{3,4}
 - 6-8% of American Women are taking MHT

Why do women discontinue MHT?

The Long View - Updated

MHT: Long-Term Mortality Adjusted Hazard Ratios

Danish registry of women from age 45

772,719 unexposed women vs 104,086 who filled MHT prescription

| | MHT/Unexposed |
|-----------------|----------------------|
| Total mortality | 0.96 (0.93 to 0.98) |
| Use < 1 year | 1.01 (0.98 to 1.03) |
| Use 1-2.9 years | 0.94 (0.89 to 0.98) |
| Use 3-4.9 years | 0.90 (0.84 to 0.95) |
| Use 5-9.9 years | 0.89 (0.84 to 0.95) |
| Use ≥ 10 years | 0.98 (0.90 to 1.07) |

Mikkelsen AP, et al. BMJ. 2026;392:e085998

Menopause 101: Key Points

- Menopause is a natural transition, albeit with a BIG impact
- Perimenopause can be chaotic and a management challenge
- Symptom onset often presents with “not feeling like myself”
- Hot flushes are more than just uncomfortable
- Bone loss begins in Perimenopause
- Genitourinary Syndrome of Menopause (GSM) is almost universal and undertreated
- Women’s Health Initiative (WHI) is widely misunderstood, and informative
- Menopause is a **“window of vulnerability and opportunity”**



THANK YOU!
QUESTIONS?

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