



Menopause and Mental Health

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INDUSTRY

Nothing to disclose

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

LEARNING OBJECTIVES

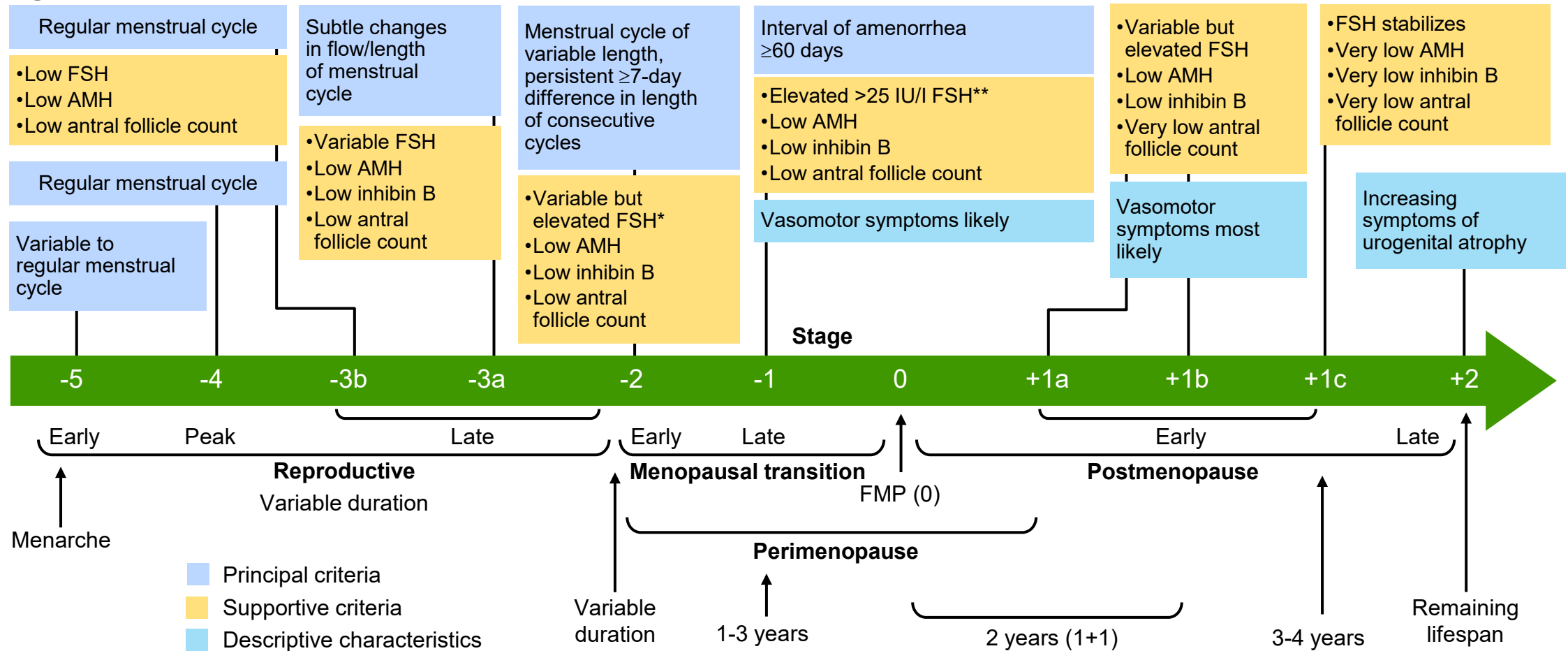
- Describe the epidemiology of the menopause transition
- Discuss mood concerns occurring in the menopause transition
- Explain HERA and DREAMS findings

Background



- Menopause
 - Defined as no menstrual cycle for 12 consecutive months
 - Mean age 52 yrs
 - Age over 45 is normal
 - 5% go through between 40-45 yrs
 - 1-3% go through before 40 yrs
- Perimenopause
 - The time leading up to menopause during which women may have symptoms
 - 6-10 years

The Stages of Reproductive Age Workshop (STRAW) +10 Staging System for Reproductive Age in Women



STRAW defined 7 stages ranging from the onset of menstrual cycles at menarche and the reproductive age to the perimenopausal and postmenopausal phases. Principal (menstrual cycle), supportive (biochemical and imaging), and descriptive (symptoms) criteria are used to characterize the phases. AMH indicates anti-Müllerian hormone; FMP, final menstrual period; and FSH, follicle-stimulating hormone. *Blood drawn on cycle days 2 to 5. **Approximate expected level based on assays using current international pituitary standard.

Symptoms associated with menopause transition

- Hot flashes
- Sleep disruption
- Joint aches
- Palpitations
- Breast pain
- Vaginal dryness
- Pain with sex
- Urinary incontinence
- Nocturia
- Brain fog/memory problems
- Mood changes including depressed mood and anxiety

Vasomotor Symptoms (hot flashes and night sweats)

- Prevalent-75% of women
- Duration
 - 7-10 years
 - Longer in women whose symptoms begin before menopause (>11 years)
 - Start earlier and last longer in Black women
 - Worse in obese women
 - 6.5% of women aged 60-65 years in a community-based sample still reported moderate-severe vasomotor symptoms



Vasomotor Symptoms

Associations

- Poorer quality of life
- Sleep problems
- Negative mood
- Lower bone density
- Future clinical cardiovascular disease (heart attack, stroke, heart failure)
- Adverse work outcomes

Risk Factors

- Low education
- Smoking
- Negative affect
- Obesity
- Adverse childhood experiences

Thurston RC, Joffe H. Obstet Gynecol Clin North Am. 2011; 38(3): 489-501. Thurston RC et al. Menopause 2008; 15(1): 16-22. Thurston RC J Am Heart Assoc. 2021 Feb 2;10(3):e017416. doi: 10.1161/JAHA.120.017416. Faubion SS et al. Mayo Clin Proc 2023; 98(6): 833-845.

MAYO CLINIC STUDY

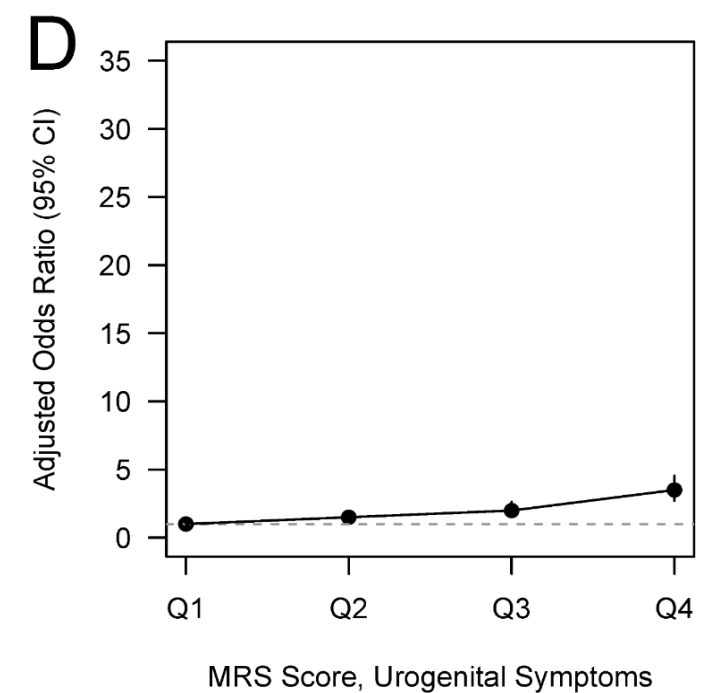
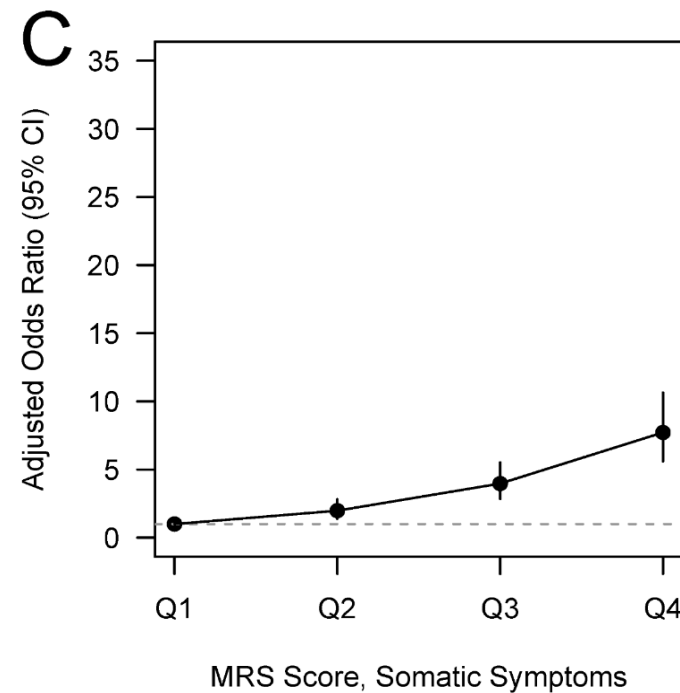
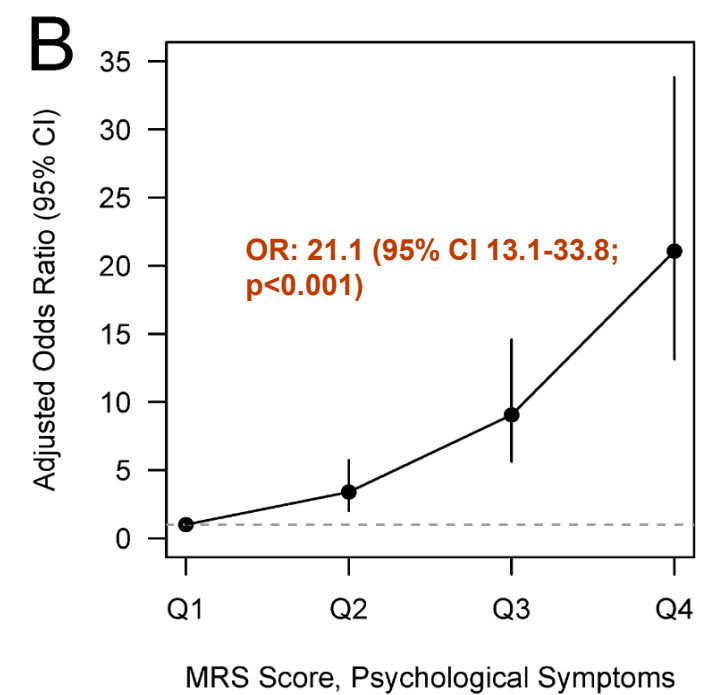
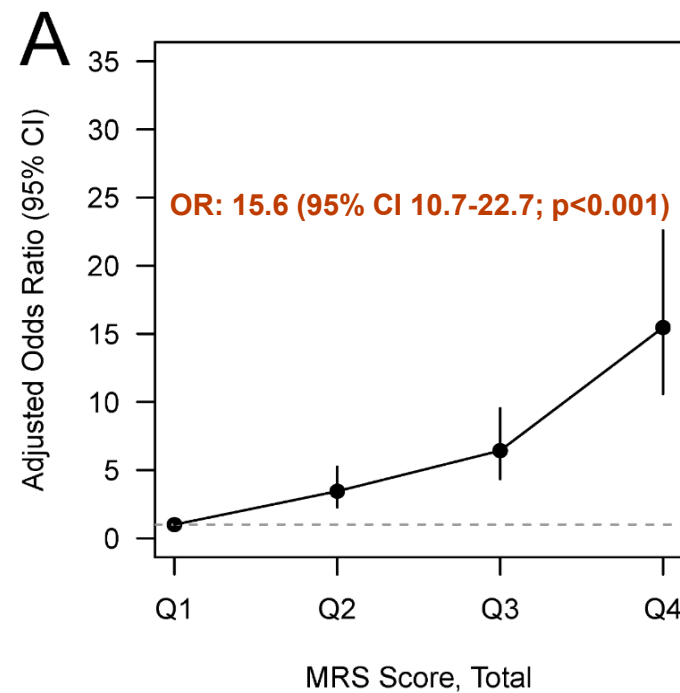
- **Hormones and ExpeRiences of Aging (HERA)**

- Cross-sectional study of women receiving primary care at 4 Mayo Clinic sites
- Participants were sent a questionnaire to assess menopause symptoms and the impact of these symptoms on work
 - Missed days from work in the past 12 months
 - Hours cut back at work in the last 6 months
 - Laid-off or fired from work in the last 6 months
 - Quit/retired/changed jobs in the last 6 months

RESULTS

- 32,469 surveys: 5,219 responses (16% response rate)
- 4,440 respondents (85%) reported current employment
 - Mean age 53.9 ± 4.5 years; majority white (93%), partnered and educated (college graduate or higher)
- Women had moderate menopause symptoms 13% of women reported at least one adverse work outcome
- 11% had missed one or more days of work in the last year ***due to menopause symptoms***
 - ***Mean number of days missed per year = 3***
 - ***Adverse work outcomes were driven by psychological symptom domain***

ASSOCIATION OF MRS SCORE QUARTILES WITH ODDS OF AN ADVERSE WORK OUTCOME DUE TO MENOPAUSE SYMPTOMS

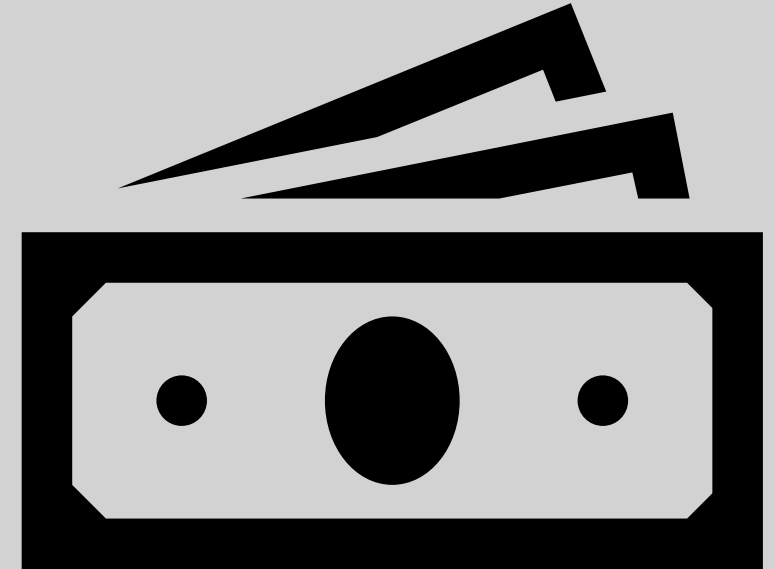


ECONOMIC IMPACT OF MENOPAUSE

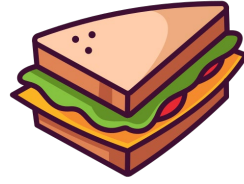
Utilizing U.S. 2020 Census data for employment and income in women 45-60 years

Cost associated with lost work productivity associated with menopause symptoms in the U.S. is at least \$1.8 billion annually

Cost including direct and indirect medical costs is estimated at \$26 billion annually!



CAREGIVING



- Women constitute 61% of caregivers in the US
- The average age of caregivers is 49.4 years
- Women are more likely to care for two or more adults than men

Typical caregivers in the US are partnered midlife women



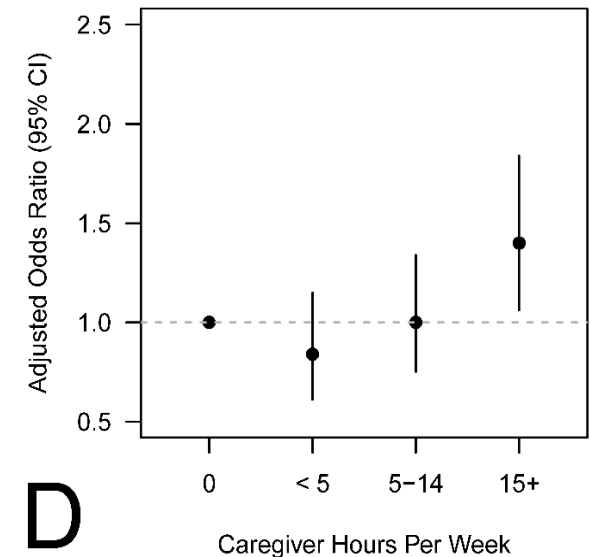
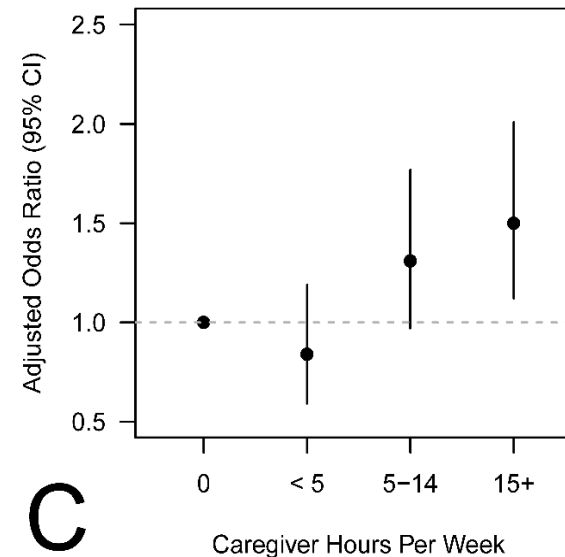
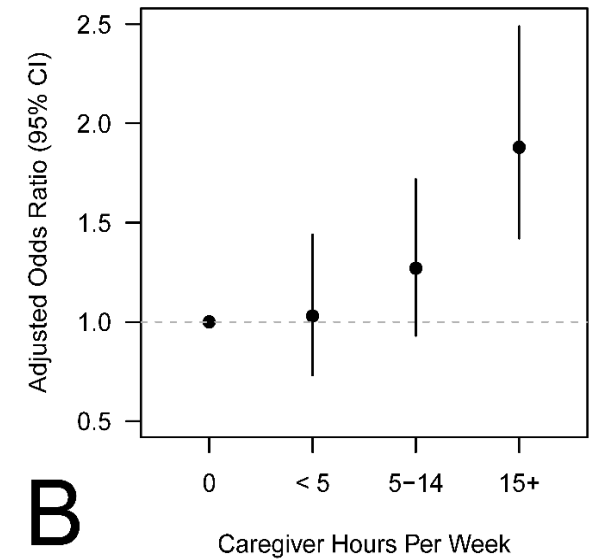
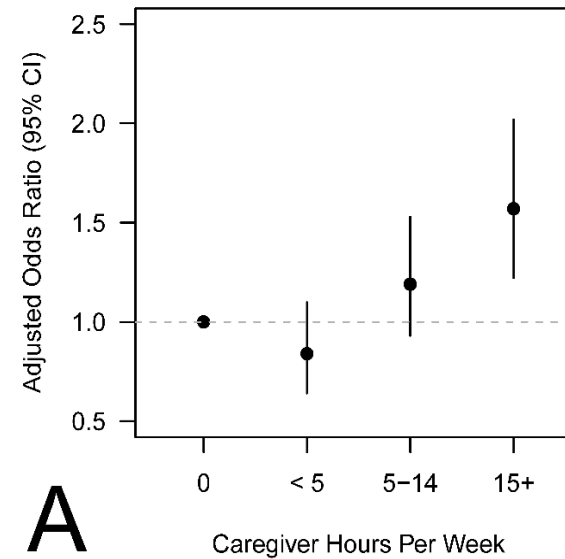
ASSOCIATION OF CAREGIVING HOURS WITH **MODERATE OR GREATER** MENOPAUSE SYMPTOM BURDEN IN:

A: At least one domain

B: Somatic domain

C: Psychological domain

D: Urogenital domain



SLEEP DISTURBANCE IN THE MENOPAUSE TRANSITION

- 2005 NIH panel reported sleep disturbance as a key perimenopausal symptom
- Menopause showed a negative effect on sleep
 - Longer sleep latency
 - Less deep sleep
- About 1 in 4 women experience insomnia
 - Women are 40% more likely to experience insomnia than men



SLEEP DISTURBANCE IN THE MENOPAUSE TRANSITION

- Vasomotor symptoms
- Loss of ovarian hormones
 - Estrogen
 - Progesterone
- Mood changes
- Weight gain
- Primary sleep disorders
 - Obstructive sleep apnea
 - Restless leg syndrome



SLEEP DISTURBANCE IN THE MENOPAUSE TRANSITION

- **Busy lifestyle**
 - Family demands
 - Work demands
- **Stress exposure**
 - Aging parents
 - Death of family/friends
 - Role transitions



DEPRESSED MOOD IN PERIMENOPAUSE

- Perimenopause is a window of vulnerability for development of depressed mood and for major depressive episodes (MDE)
- Risk of depressed mood is elevated in perimenopause even in women without a history of depression
- However, most women experiencing a MDE have had one before
- Women with hysterectomy w/ or w/o oophorectomy and those with premature ovarian insufficiency are at increased risk of depression; surgical menopause less clear

RISK FACTORS FOR MAJOR DEPRESSIVE DISORDER IN PERIMENOPAUSE

- Prior mental health issues
 - Prior MDD, current antidepressant use, anxiety, premenstrual depressive symptoms
- Sociodemographic factors
 - Black race, high BMI, younger age
- Psychosocial factors
 - Stressful life events, social isolation, role transitions
- Menopause symptoms
 - Prolonged vasomotor symptoms
 - Sleep disturbance

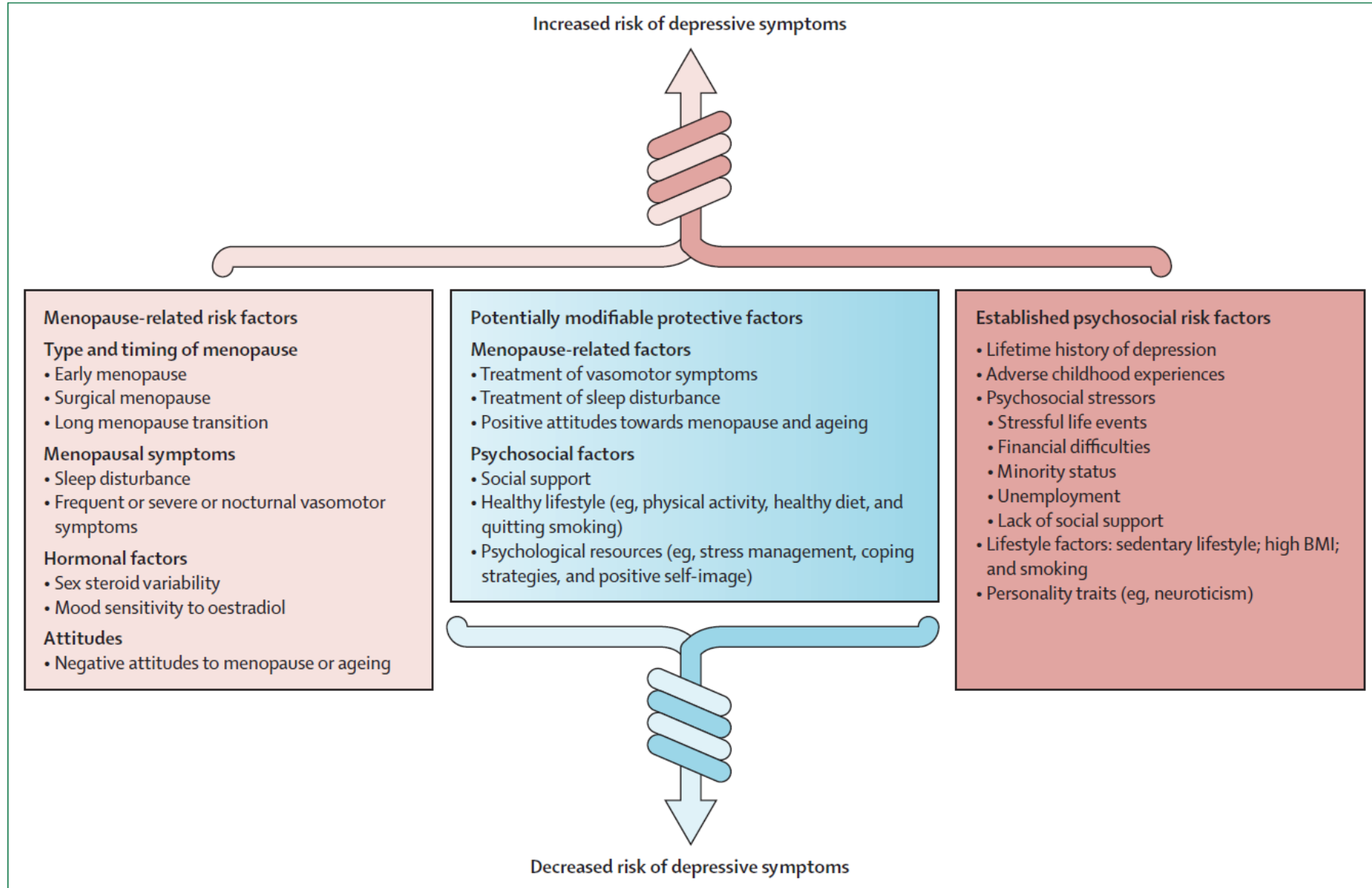


UNIQUE CHALLENGES IN MIDLIFE WOMEN



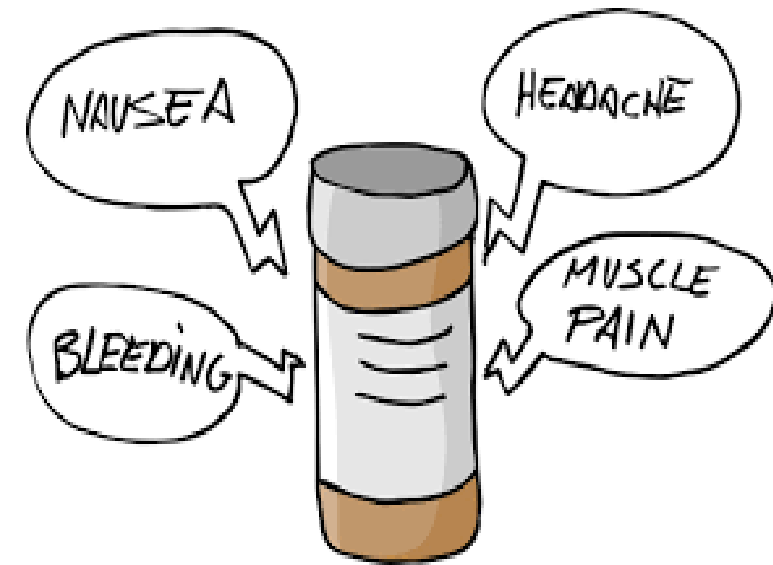
- Hot flashes, night sweats
- Sleep disruption
- Musculoskeletal health issues (joint aches, arthritis, fibromyalgia)
- Stress and busy lifestyle (sandwich generation)

MENOPAUSE AND MOOD-INTERACTION OF FACTORS



TREATMENT OF MOOD DISORDERS IN PERIMENOPAUSE

- First line therapies include proven treatments for depression (CBT, antidepressants)
- Selection of an antidepressant should consider prior trials/responses to therapy as well as efficacy and tolerability in this population
 - Attention to sexual side effects
 - Try to do “double duty” (VMS, pain)
 - Consider treating co-occurring VMS and sleep disturbances as part of treatment of depression



TREATMENT OF MOOD DISORDERS IN PERIMENOPAUSE



- There may be a “window of opportunity” for the effective use of estrogen therapy for the management of depressive disorders in perimenopause
- Estrogen has benefit ***similar in magnitude to antidepressants*** when administered to depressed perimenopausal women with or without VMS
- Estrogen is not effective as a treatment for depressive disorders in **postmenopausal** women

ANXIETY IN THE MENOPAUSE TRANSITION

- Data are mixed but overall, no consistent evidence that anxiety increases over the menopause transition
 - *Caveat: somatic anxiety might predict moderate or severe vasomotor symptoms, and reducing anxiety may reduce vasomotor symptom bother*

DATA REGISTRY ON EXPERIENCES OF AGING, MENOPAUSE AND SEXUALITY-DREAMS

- Women seen in menopause clinics at 3 geographic locations (Scottsdale, AZ, Rochester, MN and Jacksonville, FL)
- 16,220 women 2015-2022
- Investigating menopause experience and sexual health
 - Menopause symptoms (Menopause Rating Scale),
 - Mood/anxiety (PHQ-9/GAD-7),
 - Sleep (Pittsburgh Sleep Quality Index)
 - Childhood adversity (Adverse Childhood Experiences)
 - Sexual health (Female Sexual Function Index, Female Sexual Distress Scale-Revised)

DATA REGISTRY ON EXPERIENCES OF AGING, MENOPAUSE AND SEXUALITY-DREAMS

Association between menopause/vasomotor symptoms

- Social determinates of health
- Childhood adversity
- Obstructive sleep apnea
- Migraine
- Hypertensive disorders of pregnancy
- Age over 60
- Relationship distress
- Caffeine intake

Association between sexual function

- BMI
- Sleep
- Relationship satisfaction
- Resilience
- Mindfulness
- Endometriosis
- Alcohol intake
- Sexual minority women

SLEEP APNEA RISK AND VASOMOTOR SYMPTOMS



- Of 1691 women seen in our menopause clinic, 25% were intermediate or high risk for OSA on STOP BANG
- Women with severe/very severe VMS were 1.87 times more likely to be at intermediate/high risk for OSA versus those with none/mild/moderate VMS*
- Even in a subgroup analysis of women with BMI<25, OR 2.15 for intermediate/high risk for OSA in those with severe/very severe VMS

**adjusting for age, BMI, smoking status and hypertension*

SLEEP AND SEXUAL FUNCTION

- Of nearly 2500 women seen in our clinic, 75% had poor sleep quality by the Pittsburgh Sleep Quality Index, and 54% had sexual dysfunction
- On multivariable analysis, women with poor sleep quality were nearly 1.5 times more likely to report sexual dysfunction
- Good sleep quality was linked with being sexually active
- Sleep duration was not linked with sexual dysfunction
- **adjusting for age, BMI, partner status, relationship distress, education, race/ethnicity, menopause status, depression, anxiety, & HT, contraceptive, SSRI/SNRI use*



Kling JM, Kapoor E, Mara K, Faubion SS. Associations of sleep and female sexual function: good sleep quality matters. *Menopause*. 2021 Apr 19;28(6):619-625.

ADVERSE CHILDHOOD EXPERIENCES AND VASOMOTOR SYMPTOMS



- Of 1670 women with information on ACE, 977 (58%) had at least one ACE and 288 (17%) reported ≥ 4 ACEs
- There was an association between severe menopause symptoms and higher childhood adversity OR 1.8 for ACE score 1-3 and OR 4.5 for ≥ 4 vs. ACE =0
- Highlights the need to screen women for ACEs as it can impact multiple aspects of health in adulthood

**adjusting for age, partner status, education, employment, depression, anxiety, HT use*

Kapoor E, ...Faubion SS. Association of adverse childhood experiences with menopausal symptoms: Results from the Data Registry on Experiences of Aging, Menopause and Sexuality (DREAMS). Maturitas. 2021 Jan;143:209-215.

CONCLUSIONS

- Menopause is common (happens to 100% of 50% of the global population)
- There is a significant burden associated with untreated menopause symptoms
 - Vasomotor
 - Sleep
 - Mood
- Effective therapies are available and underutilized



QUESTIONS & DISCUSSION



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