Stages of Menopause

- **Premenopause**
  - Regular cycles
  - Fertility possible
  - No symptoms
- **Perimenopause**
  - Irregular cycles
  - Fertility low
  - Symptoms start
- **Menopause**
  - No cycles for 12 months
  - Fertility ends
  - Symptoms worsen

The Perimenopausal Transition

- Average age of onset: 46 years
- Age of onset for 95% of women: 39-51 years
- Average duration: 5 years
- Duration for 95% of women: 2-8 years1

1. Fritz MA, Speroff L. *Clinical Gynecologic Endocrinology and Infertility*. 8th ed. LWW; 2011.

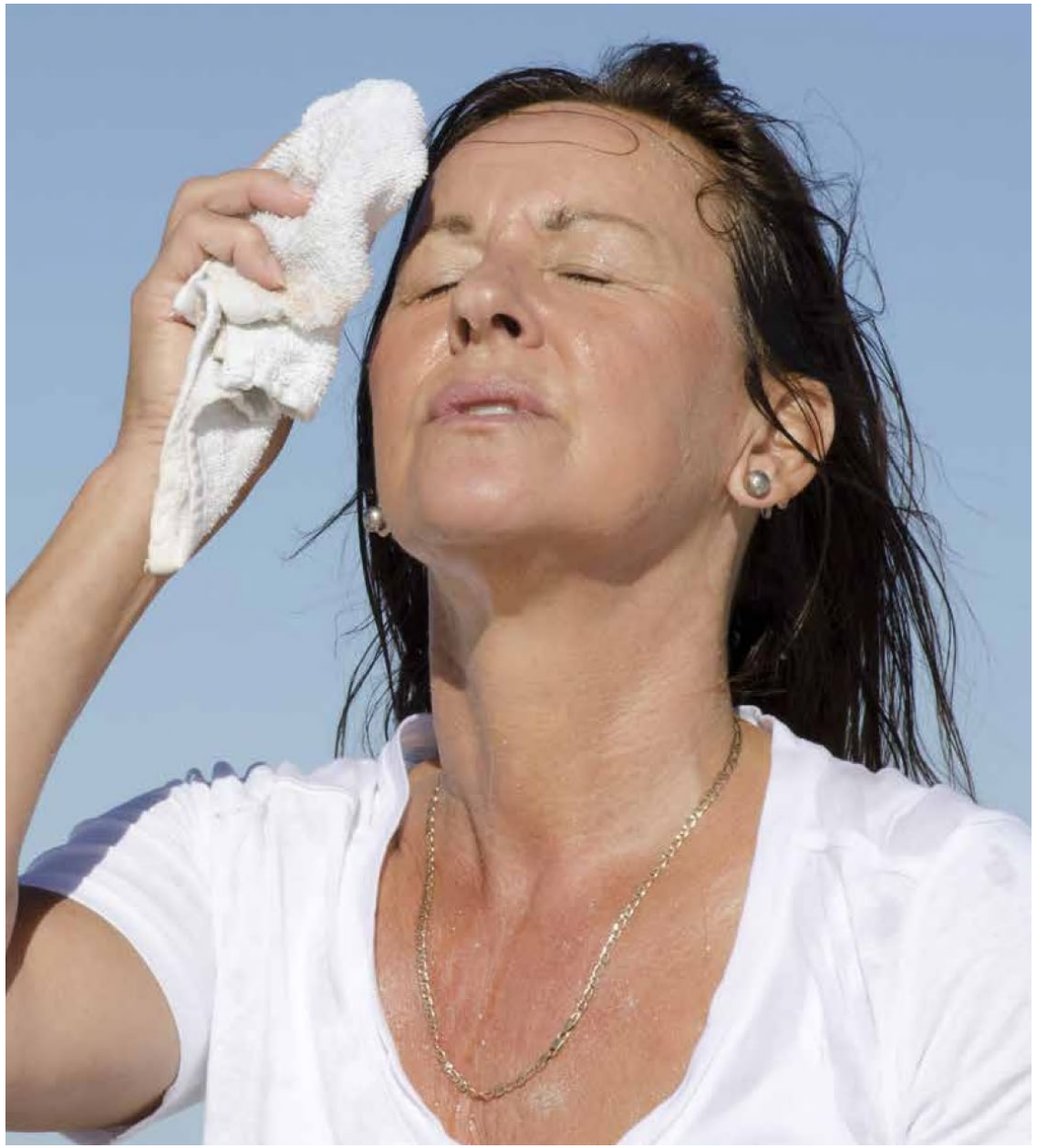
Any 3 Define Onset of Perimenopause

- New heavy or longer flow
- Shorter menstrual cycle lengths (<25 days)
- New breast tenderness or fibrocystic changes
- New or increased dysmenorrhea
- New mid-sleep awakening
- Onset of night sweats, especially around menses
- New or increased migraine headaches
- New or increased premenstrual mood swings
- Weight gain without changes in exercise or food intake

Prior JC, et al. *BC Med J*. 2005;47:534-538.

Menopause = Estrogen Deficiency State

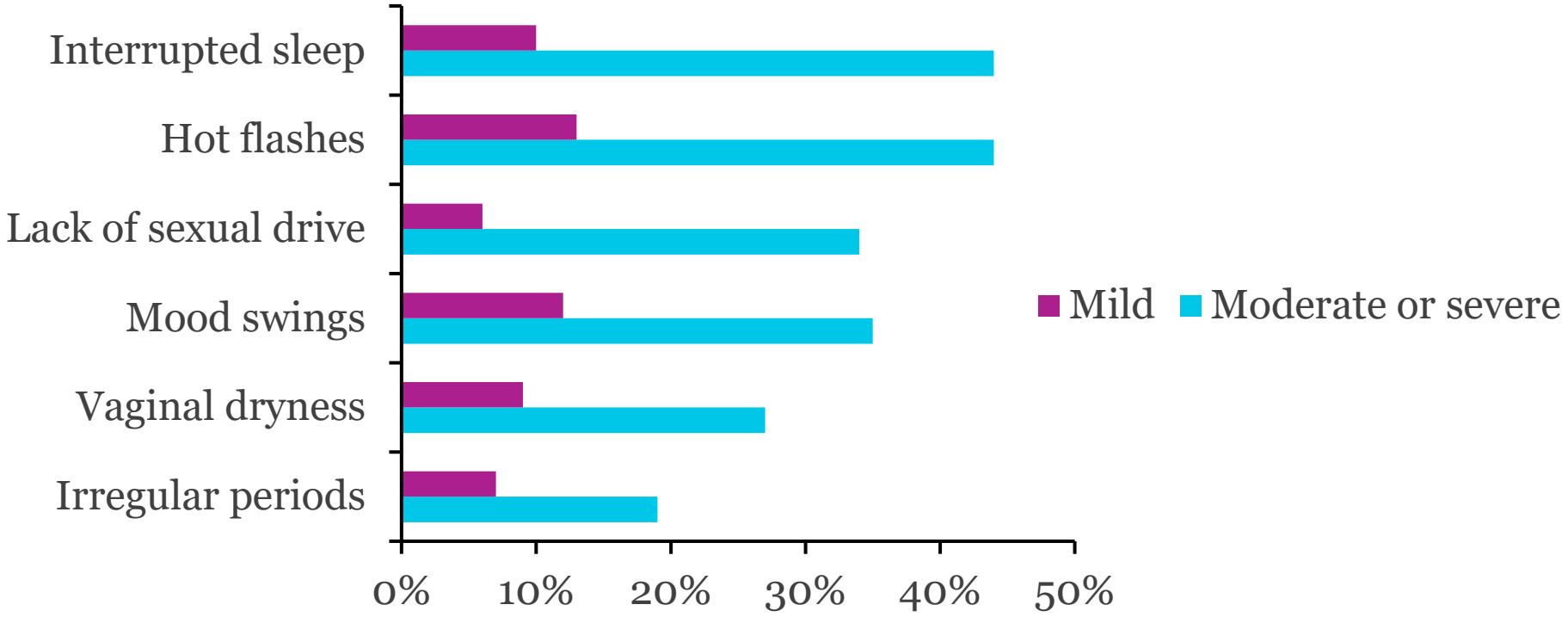
- Multiple organ impact:
  - Skin
  - Skeletal
  - Genitourinary
  - Cardiovascular
  - Central nervous system



Vasomotor Symptom Complex

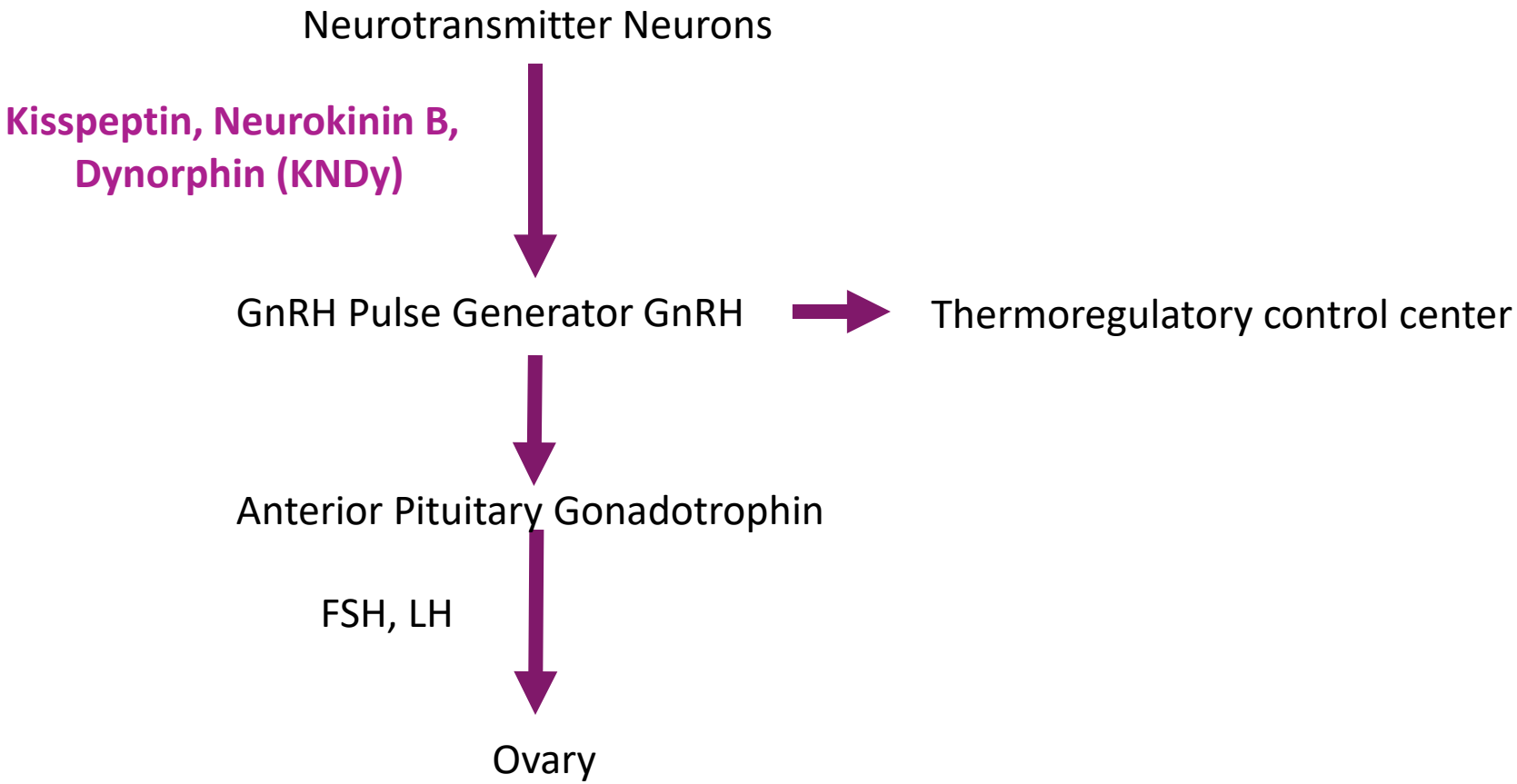
- Heart rate increases
- Respiratory rate increases
- Sudden sensation of warmth
- Flush begins in thorax and neck and extends to face and down arms
- Profuse perspiration follows in same area
- Women can perceive flash before any of the characteristic changes can be measured
- Nonspecific complaints that result from sleep disruption and interruption: irritability, anxiety, nervousness, depression, fatigue, forgetfulness, and inability to concentrate

Percentage of Women Currently Experiencing Menopause Symptoms

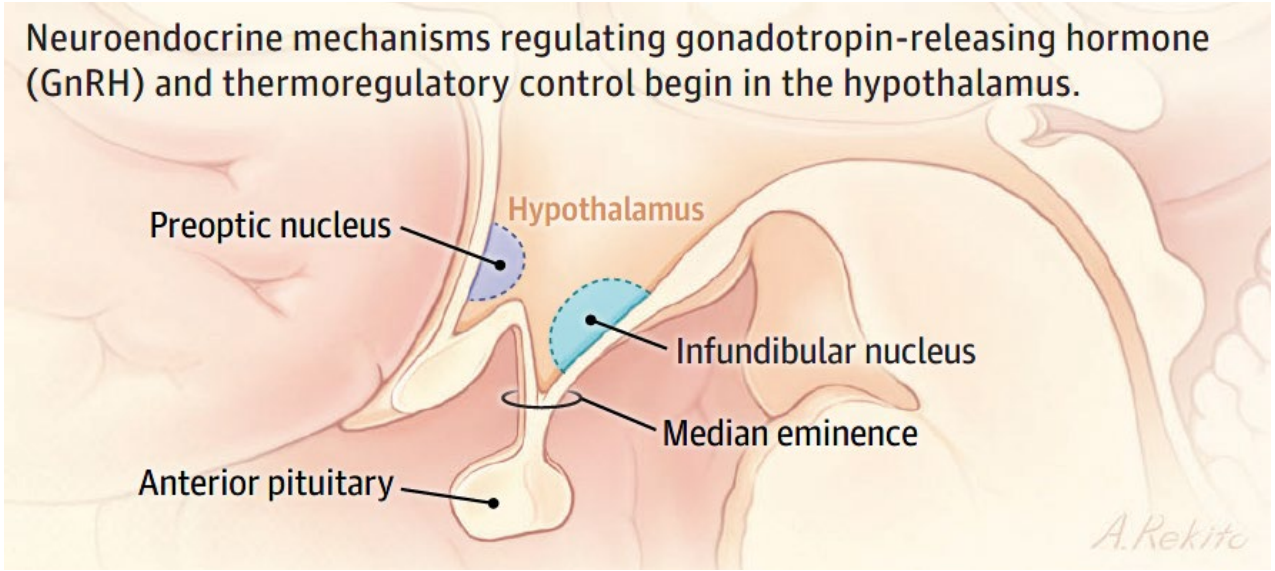


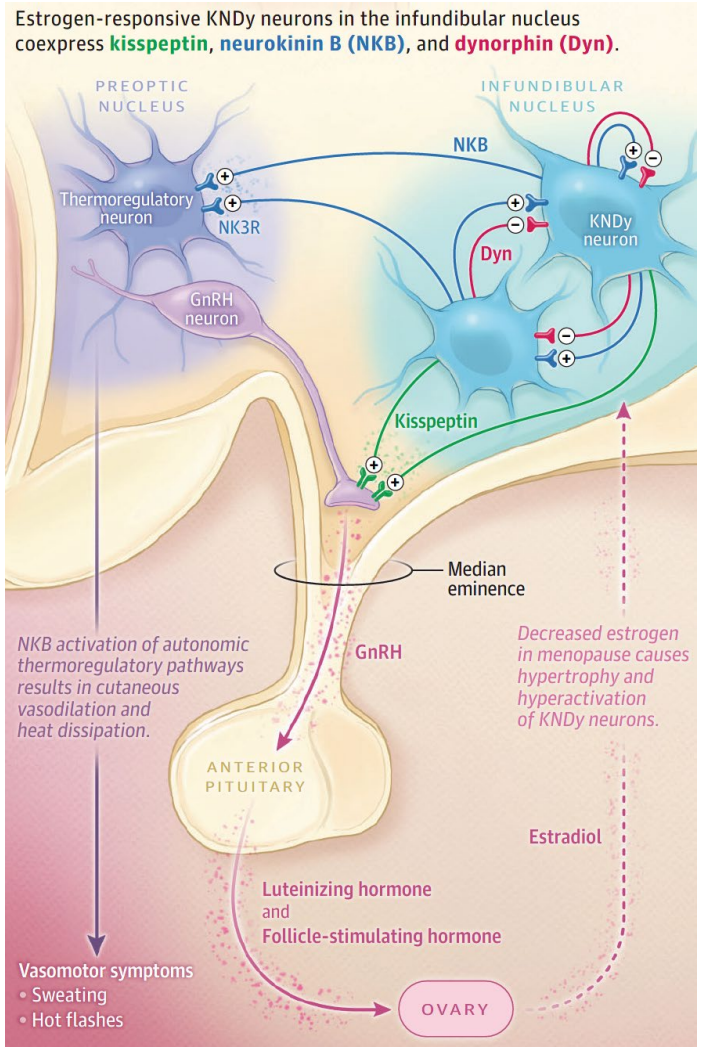
Slide Courtesy of Dr. Anita Nelson.

More Complete Picture of H-P-O



Mediation of gonadotropin release and thermoregulatory control through hypothetical neuroendocrine mechanisms





Christ JP, et al. JAMA. 2023;330(13):1278-1279.

Women's Health 2023
Beyond the Annual Visit

Slides for 1C

Menopausal Mornings

- Sleep Disorders
- Perimenopause: 16%-47%
- Menopause: 35%-60%
- Female gender is an independent risk factor for insomnia
- Women report insomnia 1.4 times as often as men

Tandon VR, et al. *J Midlife Health*. 2022;13(1):26-33.
Soares CN, Murray BJ. *Psychiatr Clin North Am*. 2006;29(4):1095-1113.

Deep Delta Wave Sleep

- Slow-wave sleep – 60 to 90 minutes/night
- When the body releases growth hormone to repair and stimulate the growth of tissue, bone, and muscle
- Helps strengthen the immune system
- Helps regulate glucose metabolism

Hilditch CJ, McHill AW. Nat Sci Sleep. 2019;11:155-165.

Sleep Fragmentation

- **VMS-Induced**
- **Sleep Cycle Disruptions**

- While asleep: mini-awakenings
- 2-10 times as often as becoming fully alert
- Moving out of delta wave sleep multiple times into lighter sleep
- Leads to reductions in total restorative sleep

Joffe H, et al. *Menopause*. 2013;20(9):905-914.

Productivity

- 67% of women experience brain fog
- 1 in 4 consider leaving their jobs because of impaired productivity
- 1 in 10 do
- Presenteeism – women with more severe symptoms; 90% report a negative impact on their performance
- Mayo clinic study: lost productivity in the workplace; an estimated $1.8 billion in lost work time per year and $26.6 billion annually when medical expenses are added, in the US alone

Faubion SS, et al. *Mayo Clin Proc.* 2023;98(6):833-845.

QOL – Intimacy

Whether in a partnered relationship or flying solo, intimacy, satisfaction, and sexual response change

Every aspect of life is impacted

Hormonal Options for Menopause

- Key points: All hormones are NOT created equal
- Route of delivery impacts side effects and risks
- In general, the benefits of hormonal therapy far outweigh potential risks
- There is a difference between systemic and local (vaginal) hormone treatment

Hormone Therapy Terminology

- *Hormone therapy* (HT) is the only pharmacologic therapy government- approved in the US and Canada for treating menopausal symptoms. HT encompasses both estrogen-alone and estrogen-progestogen therapies.
- *Estrogen therapy* (ET): Unopposed estrogen is prescribed both a) systemically for women who do not have a uterus, and b) locally in very low doses for any woman with vaginal symptoms
- *Estrogen-progestogen therapy* (EPT): Progestogen is added to ET to protect women with a uterus against endometrial cancer, which can be caused by estrogen alone
- *Bioidentical hormone therapy* (BHT): Consists of hormones chemically identical or very similar to those made in the body. Available from 2 sources: 1) FDA-approved and tested; 2) unapproved and untested from compounding pharmacies

Hormone Therapy: What We Know Today
All Estrogens Are NOT Created Equal

- HT formulation, route of administration, and timing of initiation produce different effects (eg, transdermal route may carry lower risk for thrombosis)
- Absolute risks for HT use in healthy women ages 50-59 are low but can include thrombosis, stroke, and cardiovascular events
- HT initiation in older women carries greater risks (women > 10 years from final menstrual period)
- Breast cancer risk increases with EPT beyond 3-5 years
- ET alone can be considered for longer duration of use because it carries a lower risk for breast cancer
- Consider each woman's priorities and risk factors prior to initiating HT

Efficacy of Estrogen Therapy Hot Flashes (cont'd)

- *All types of estrogen are effective for relieving hot flashes.*
- "In a meta-analysis of 24 trials of menopausal estrogen in 3329 postmenopausal women, the frequency of hot flashes decreased more in those receiving estrogen (weighted mean difference -18 hot flashes per week compared with placebo; 95% CI -22.86 to -12.99; 75 percent reduction)."
- "The severity of hot flashes also decreased more with estrogen compared with placebo."

Martin KA, Barbieri RL. Treatment of menopausal symptoms with hormone therapy. In: Crowley WF Jr, ed. UpToDate. UpToDate, Inc; 2023.

Efficacy of Estrogen Therapy Hot Flashes (cont'd)

- *All types of estrogen are effective for relieving hot flashes.*

- In a second meta-analysis, equivalent doses of different estrogens (17-beta estradiol [oral 1 mg/day or transdermal 0.05 mg/day] and conjugated estrogen 0.625 mg/day) appeared to be equally effective for the treatment of hot flashes.

- These doses eliminate hot flashes completely in approximately 80 percent of women and reduce the frequency and severity in the remainder.

Martin KA, Barbieri RL. Treatment of menopausal symptoms with hormone therapy. In: Crowley WF Jr, ed. UpToDate. UpToDate, Inc; 2023.

Who Might Want Prescription Nonhormonal Approaches?

- Symptomatic people who
  - have medical contraindications to hormonal therapy.
  - have not responded to behavioral and/or OTC approaches.
  - are hesitant/opposed to use hormone therapy (HT) or
  - may wish to know that they need HT.
  - have less severe symptoms.

Nonhormonal Options: NAMS 2023
Treatment of Vasomotor Symptoms

- Evidence-based review of the literature resulted in several nonhormone options
- **Recommended:**
  - **Level I**: cognitive-behavioral therapy, clinical hypnosis, selective serotonin reuptake inhibitors/serotonin-norepinephrine reuptake inhibitors, gabapentin, fezolinetant
  - **Level I-II**: oxybutynin
  - **Levels II-III**: weight loss, stellate ganglion block

North American Menopause Society. *Menopause*. 2023;30(6):573-590.

Dosing Ranges for *Nonhormonal* Drugs

Paroxetine salt	Brisdelle	7.5-10.0 mg	Single dose, no titration needed
Paroxetine	Paxil	7.5-25 mg	Start with 7.5-100 mg/d
Citalopram	Celexa	10-20 mg	Start with 10 mg/d
Escitalopram	Lexapro	10-20 mg	Start with 10 mg/d (for sensitive or older women, start with 5 mg/d)
Desvenlafaxine	Pristiq	100-150 mg	Start with 25-50 mg/d and titrate up by that amount each day
Venlafaxine	Effexor	37.5-150 mg	Start with 37.5 mg/d
Gabapentin	Neurontin	900-2,400 mg	300 mg at night, then add 300 mg at night, then a separate dose of 300 mg in the morning

North American Menopause Society. Menopause. 2015;22(11):1155-1172.

VMS: *Nonhormonal* Therapies

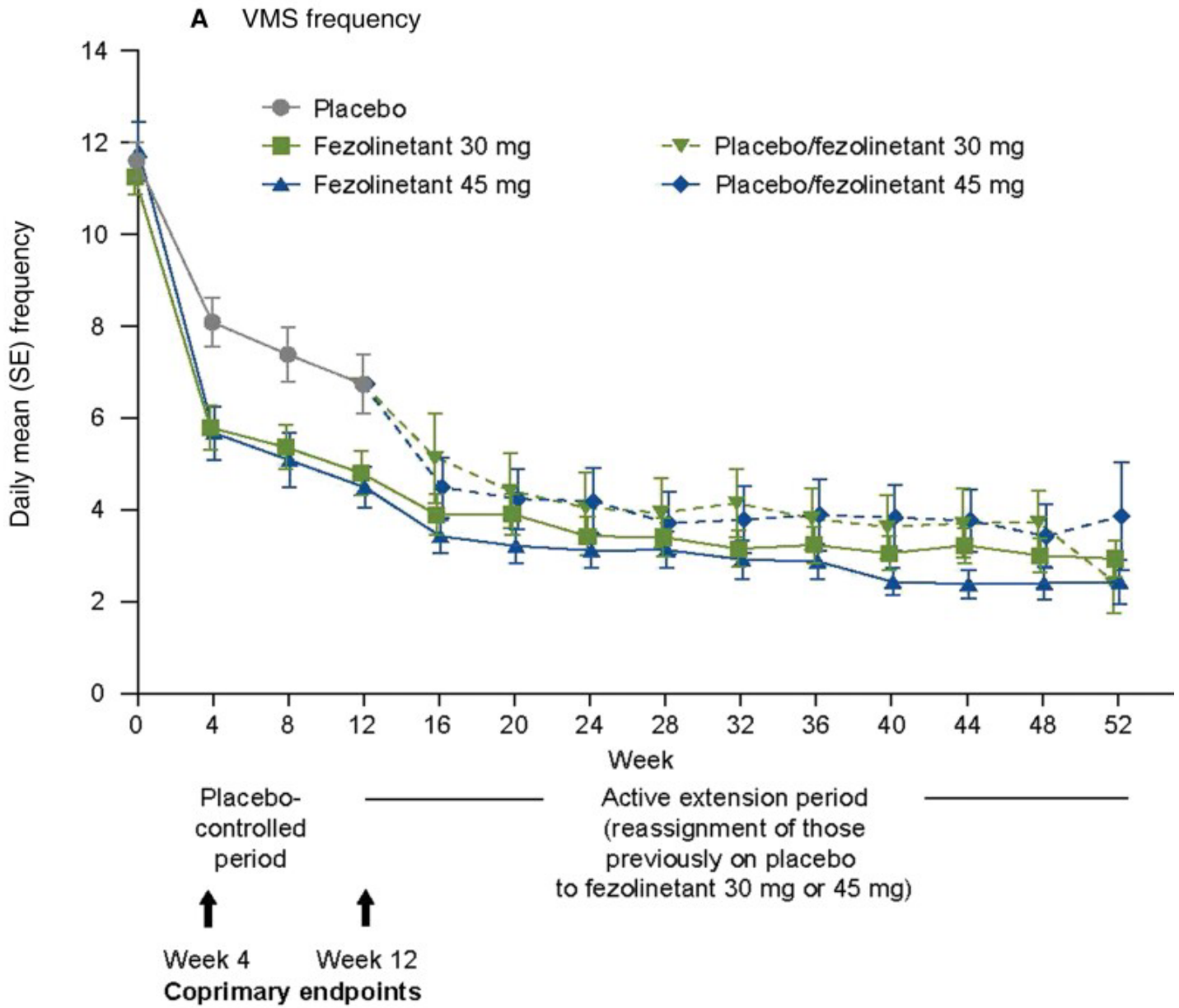
	% treated pts with >50% ↓HF	% placebo pts with >50% ↓HF
Venlafaxine 75 mg	54%-70%	30%
Paroxetine 10 mg	50%-76%	35%-57%
Sertraline	40%-56%	21%-41%
Escitalopram	55%	36%
Gabapentin	46%-84%	27%-47%

Loprinzi CL, et al. *J Clin Oncol*. 2009;27(17):2831-2837.

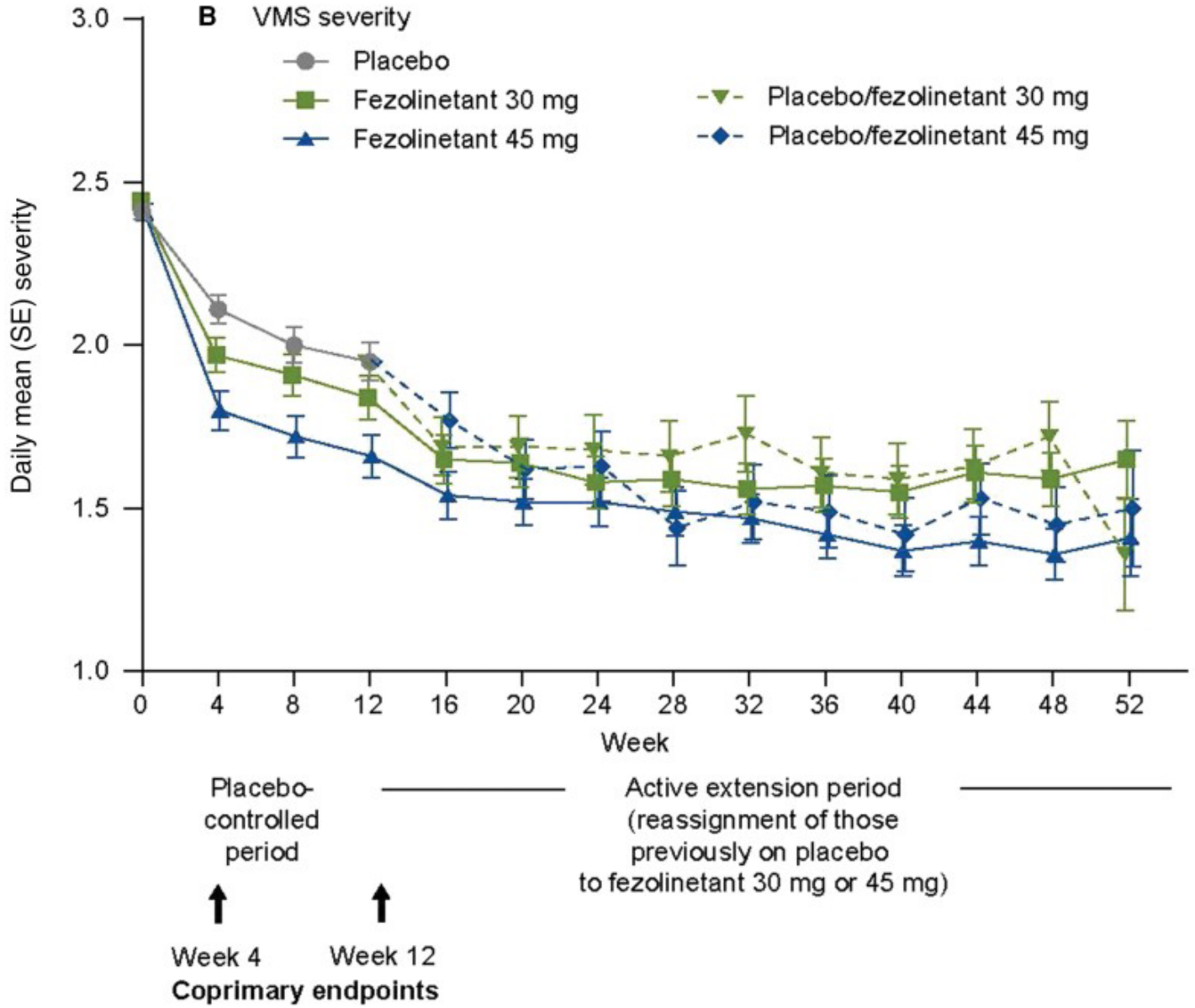
Neurokinin 3 Receptor (NK3R) Antagonists

- CNS network of kisspeptin, neurokinin, and dynorphin (KNDy) neurons in hypothalamic preoptic nucleus involved in regulating body temperature by activating NK3R
- Fezolinetant antagonizes NK3R: VMS frequency reduced
  - 30-mg dose, 56% reduction
  - 45-mg dose, 61% reduction
  - Placebo, 35% reduction
- Severity of VMS was also reduced more than placebo
- Increases in LFTs seen in 1%-6% of users; need to test baseline

Lederman S, et al. *Lancet*. 2023;401(10382):1091-1102.



Johnson KA, et al. *J Clin Endocrinol Metab*. 2023;108(8):1981-1997.



Johnson KA, et al. *J Clin Endocrinol Metab*. 2023;108(8):1981-1997.

Gender Inclusive Approach

- Acknowledge that many individuals with menopausal symptoms do not identify as a woman
- It's essential to create an environment where all individuals feel welcomed, affirmed, and able to access care
- Don't assume anatomy or identity
- If appropriate, using an organ inventory can help the clinician better understand where the person is in their journey

Wesp L. Transgender patients and the physical examination. June 17, 2016. https://transcare.ucsf.edu/guidelines/physical-examination

L G B T Q Q Definitions

- LGB – Lesbian, Gay, Bisexual
  - Cisgender: Identifies with sex assigned at birth
- T – Transgender
  - Trans man: A person assigned female sex at birth but who identifies as a man
  - Trans woman: A person assigned male sex at birth but who identifies as a woman
- QQ – Queer and Questioning
  - Genderqueer: A gender identity that rejects the notion that all genders can be described using the masculine/feminine binary

Start the Discussion

- Introduce yourself with your preferred pronouns, ask which they prefer
- List of medications and OTC used
- Organ inventory – what is present and what primary care recommendations to make
- Any GAHT – Gender-affirming hormone treatment
- Any GAST – Gender-affirming surgical treatment

Hormonal Fluctuations to Keep in Mind

- Estrogen is used to feminize
- If there's an interruption prior to surgery, symptoms can start
- 5α-reductase inhibitors (finasteride) inhibit testosterone and DHT
- Leuprolide – GnRH agonist can also lead to hot flashes

Gender Inclusiveness Resources

Ongoing continuing education: Fenway Institute
https://www.lgbtqiahealtheducation.org/

Online providers: Folx
https://www.folxhealth.com/gender-affirming-care

Asking the Right Questions

- Have you had any bleeding in the last 12 months? No – menopause, Yes – peri or pre
- Can you describe the frequency/length of periods?
- Can you describe what you're experiencing?
- What is your biggest concern?
- What have you tried, what works? Doesn't?

What Brings You In?

- I'd like to know a little bit more about your:
  - Sleep
  - Mood
  - Memory
  - Weight
  - Other
  - Sexual health
  - Vaginal symptoms
  - Bladder/urinary tract
  - Muscle/joint aches