Patient-Centered Approaches to Contraception in Perimenopause

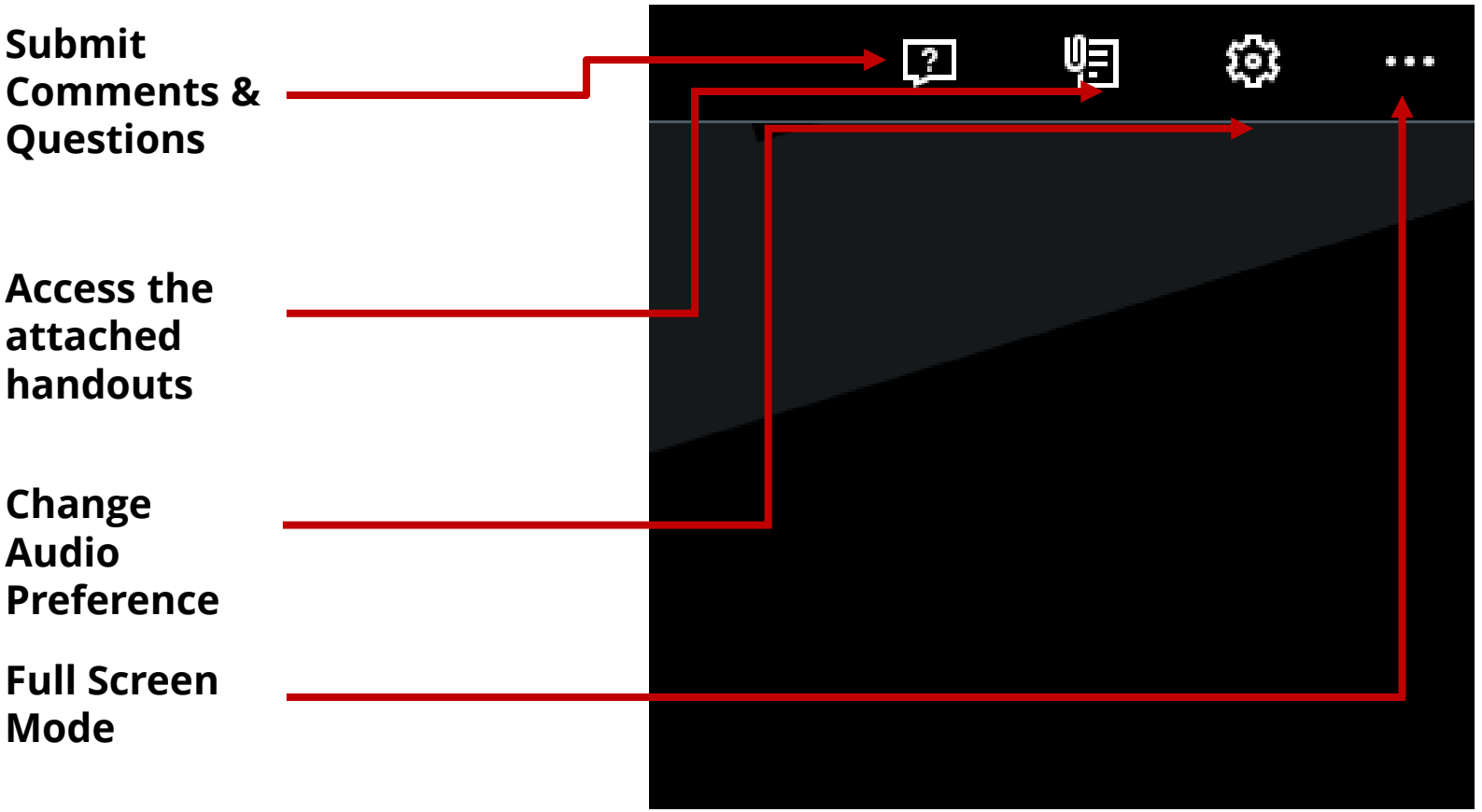
Jennifer Karlin, MD, PhD

DHCS
CALIFORNIA DEPARTMENT OF HEALTH CARE SERVICES

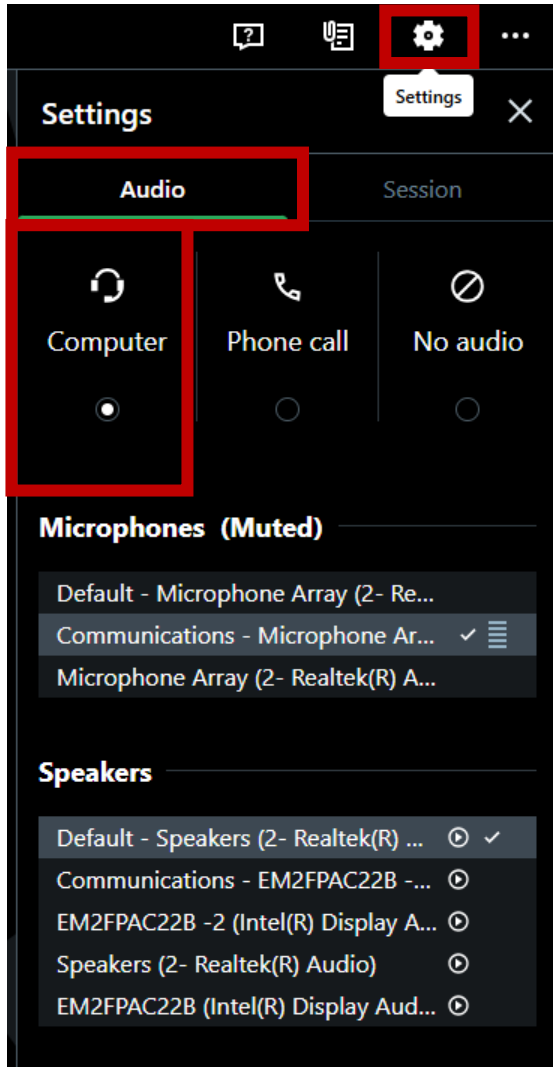
CAPTC
California Prevention Training Center

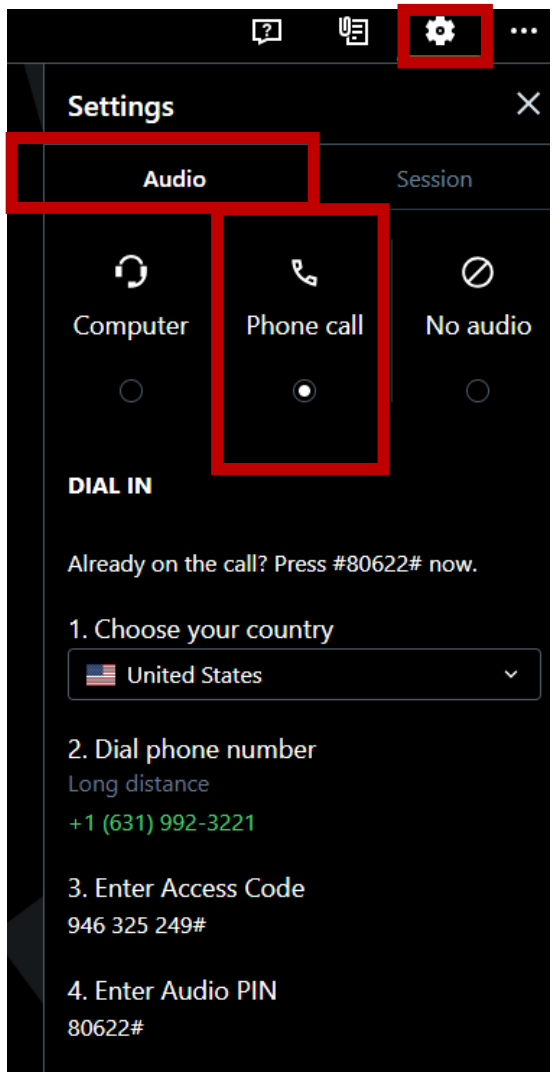
August 26, 2025

GoToWebinar Housekeeping: Attendee Dashboard

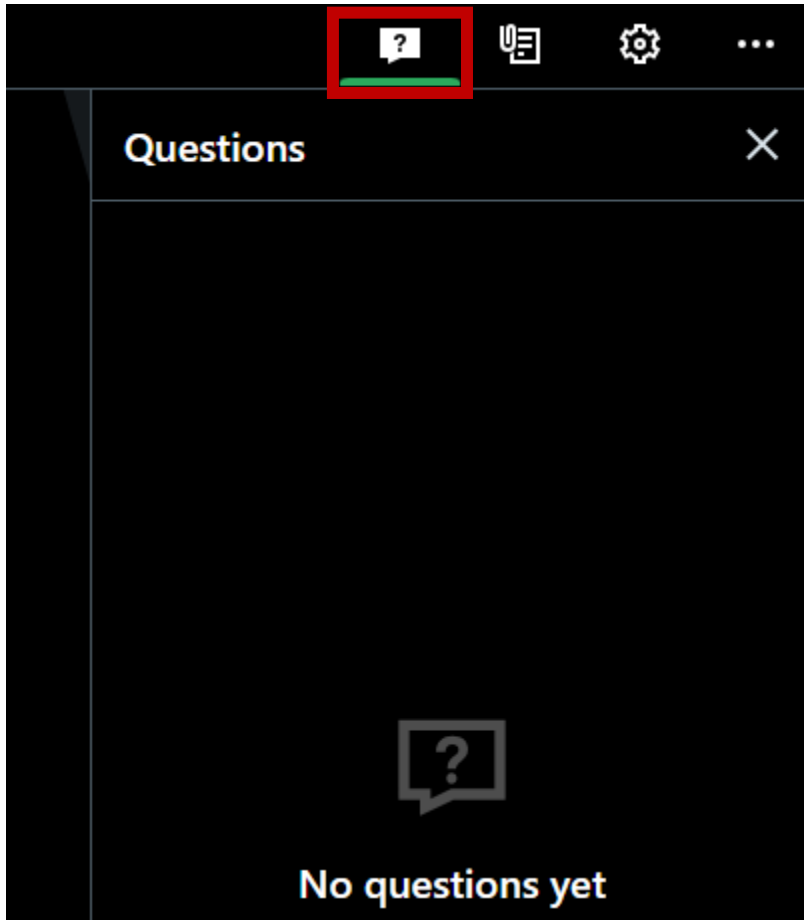


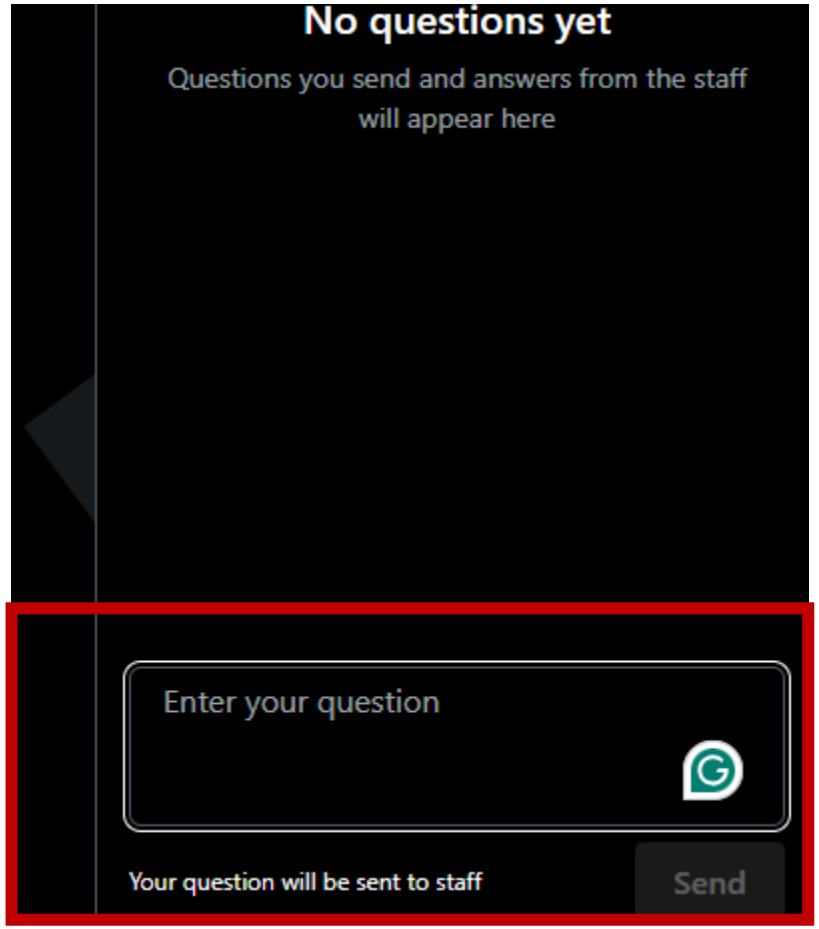
GoToWebinar Housekeeping: Audio





GoToWebinar Housekeeping: Submitting Questions and Comments





Disclosure Policy

- As an accredited provider of continuing medical education through the Accreditation Council for Continuing Medical Education (ACCME) the University of Nevada, Reno School of Medicine must ensure balance, independence, objectivity, and scientific rigor in all its educational activities. In order to assure that information is presented in a scientific and objective manner, The University of Nevada, Reno School of Medicine requires that anyone in a position to control or influence the content of a continuing medical education activity disclose relevant financial relationships with any commercial or proprietary entity producing health care goods or services relevant to the content being planned or presented. Following are those disclosures.

Presenter Disclosure

- All presenters, planners or anyone in a position to control the content of this continuing medical education activity have indicated that neither they nor their spouse/legally recognized domestic partner has any financial relationships with commercial interests related to the content of this activity.

Michael Policar, MD, MPH (Q&A Moderator)

- Professor Emeritus, Department of Obstetrics, Gynecology & Reproductive Sciences, University of California, San Francisco School of Medicine
- Clinical Fellow, National Family Planning and Reproductive Health Association (NFPRHA)

Jennifer Karlin, MD, PhD

- Associate Professor, Department of Family & Community Medicine, University of California, San Francisco School of Medicine
- Medical Consultant for the CA Family PACT Program, California Prevention Training Center
- Associate Editor, *Annals of Family Medicine*

Jennifer Karlin, MD, PHD

- No disclosures
- Acknowledgment: Michael Policar, MD, and to Contraceptive Technology 22nd Edition, Chapter 21, written by Amanda Black, MD/MPH, Alexandra Sherman, WHNP-BC/MSCP, and Taniqua A. Miller MD/MSCP

Session Aims

- Define and understand the pathophysiology of menopause and perimenopause
- Describe the most common menopausal symptoms
- Support patient-centered approach to management of menopause and perimenopausal symptoms

Define and Understand

Define and understand the pathophysiology of menopause and perimenopause

Menopause Terms

- Menopause
  - *The date* of a woman's **final menstrual period (FMP)**
  - After the FMP, **12 months of amenorrhea are required to establish the diagnosis of menopause**
- Menopausal Transition (MT)
  - The time before the FMP when menstrual cycles exhibit variability between cycles
  - A persistent difference of a minimum of 7 days in length of consecutive menstrual cycles, where the 7-day differences occur within 10 cycles of the first variable cycle
- Perimenopause
  - Interval from the onset of menopausal symptoms until one year after the final menstrual period
  - Characterized by oligo- and anovulation with irregular cycles, and an increase in psychosocial symptoms (mood swings, anxiety, memory changes, sleep disturbances, "brain fog"), variable vasomotor symptoms (hot flashes, night sweats)

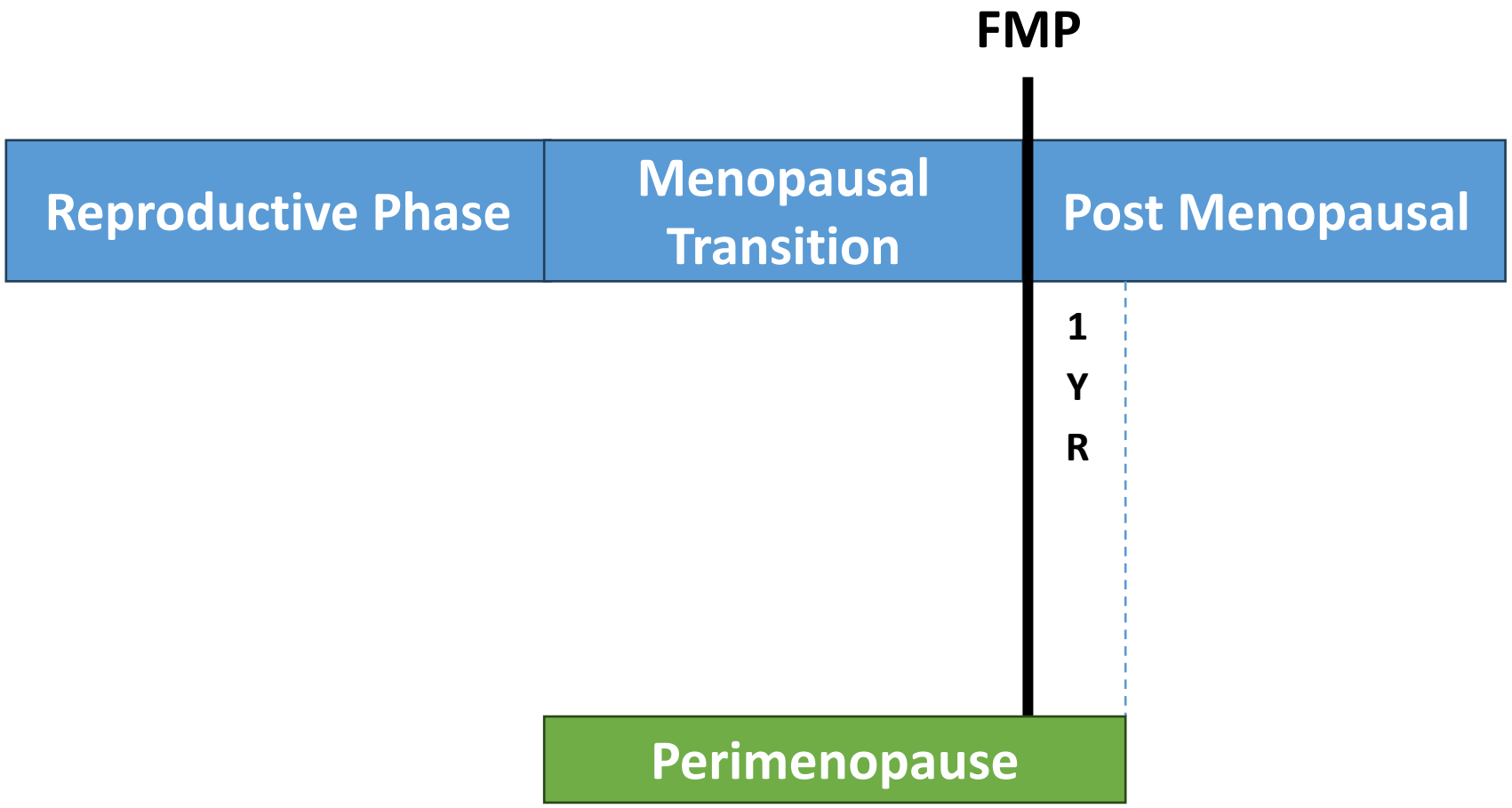
Simpson. N. Y. Acad. Sci., 2008., Persani, L. et al. J. Mol. Endocrinol, 2010, Cordts, E. B. et al., Arch. Gynecol. Obstet. 2011., Paramsothy et al., Menopause, 2017.

Stages of Reproductive Aging Workshop (STRAW)

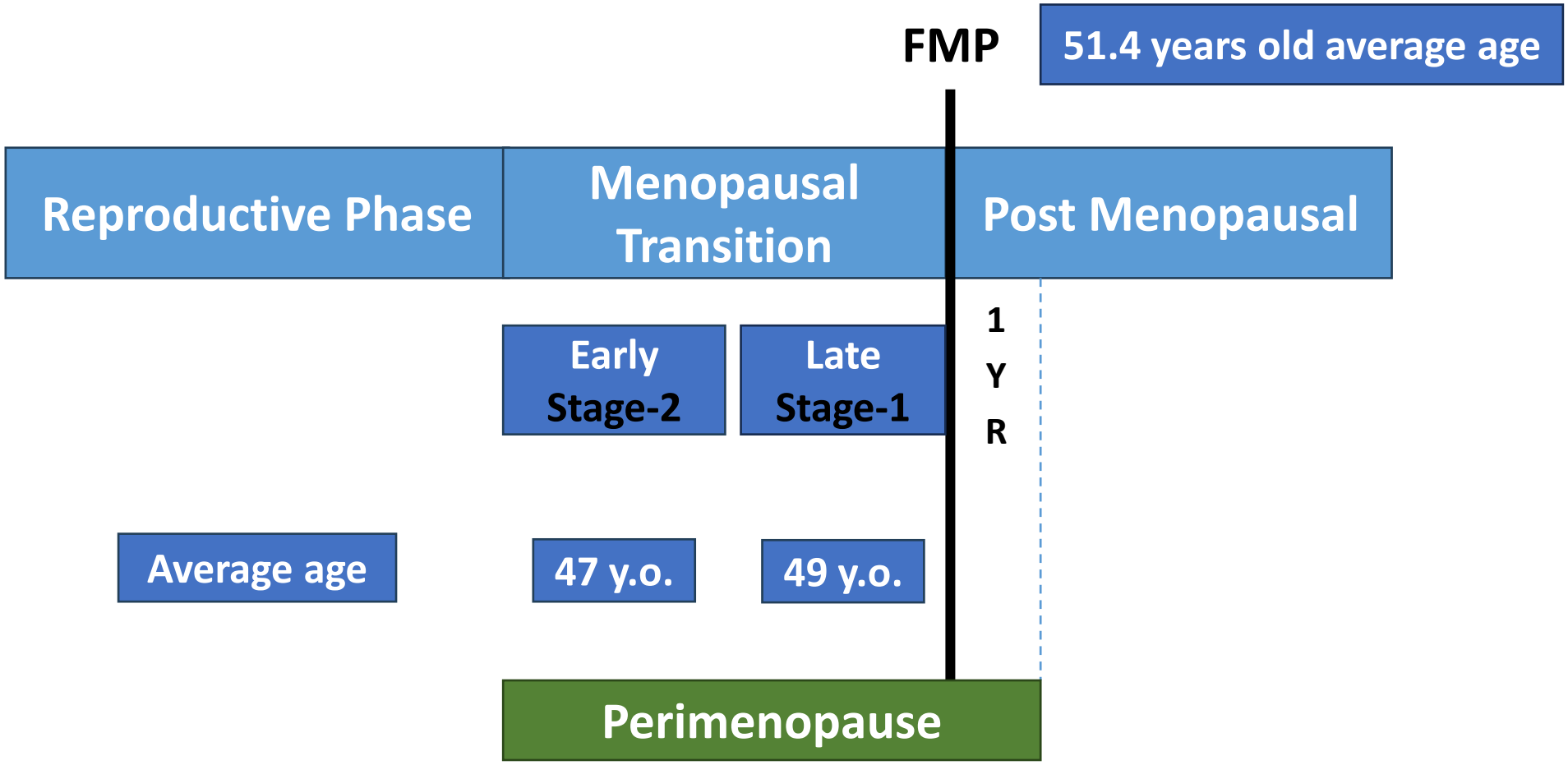
Menarche — **FMP (0)**

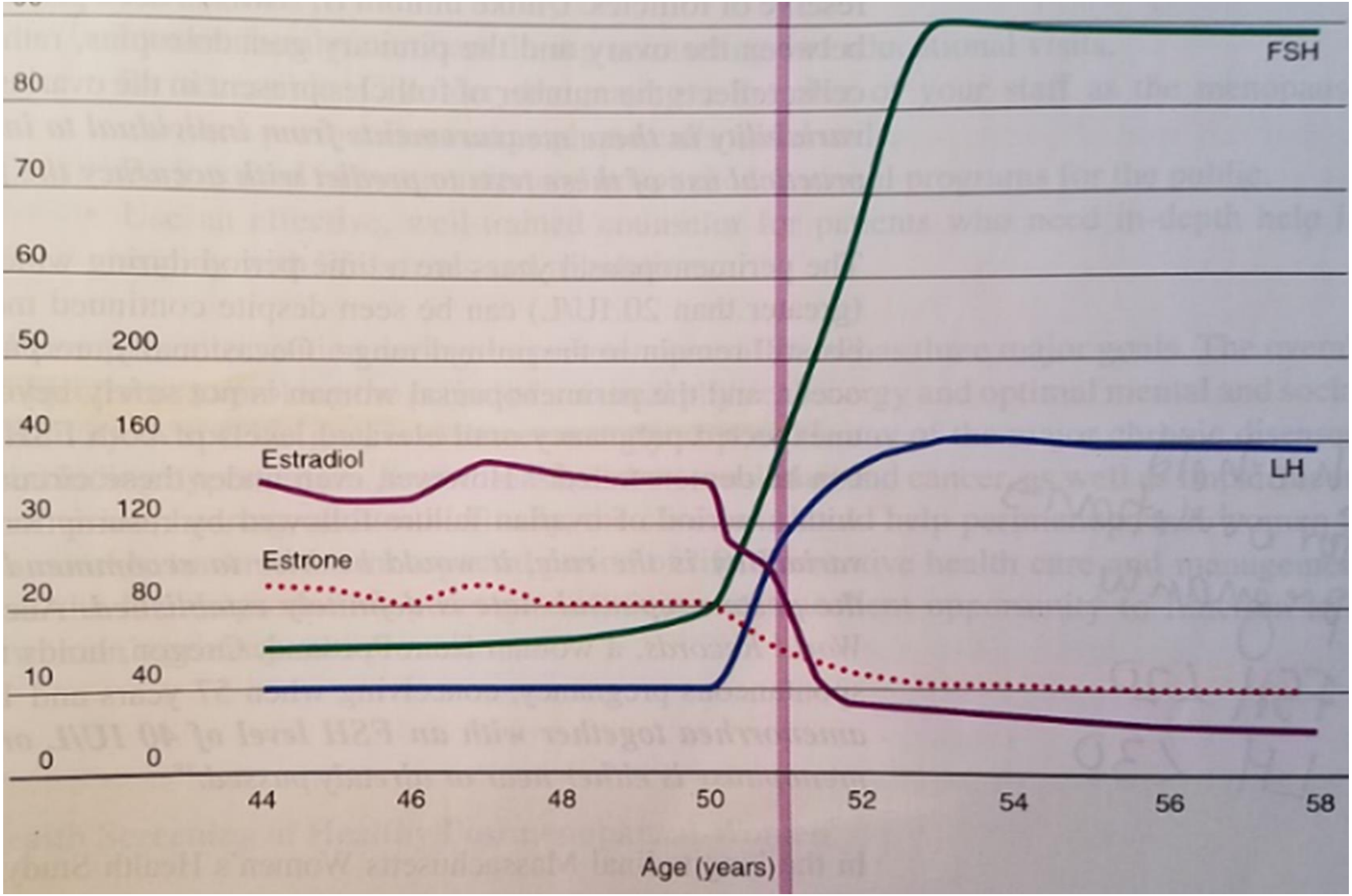
Stage	-5	-4	-3b	-3a	-2	-1	+1a	+1b	+1c	+2
Terminology	**REPRODUCTIVE**				**MENOPAUSAL TRANSITION**		**POSTMENOPAUSE**			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	*variable*				*variable*	1-3 years	2 years (1+1)		3-6 years	*Remaining lifespan*
PRINCIPAL CRITERIA										
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				

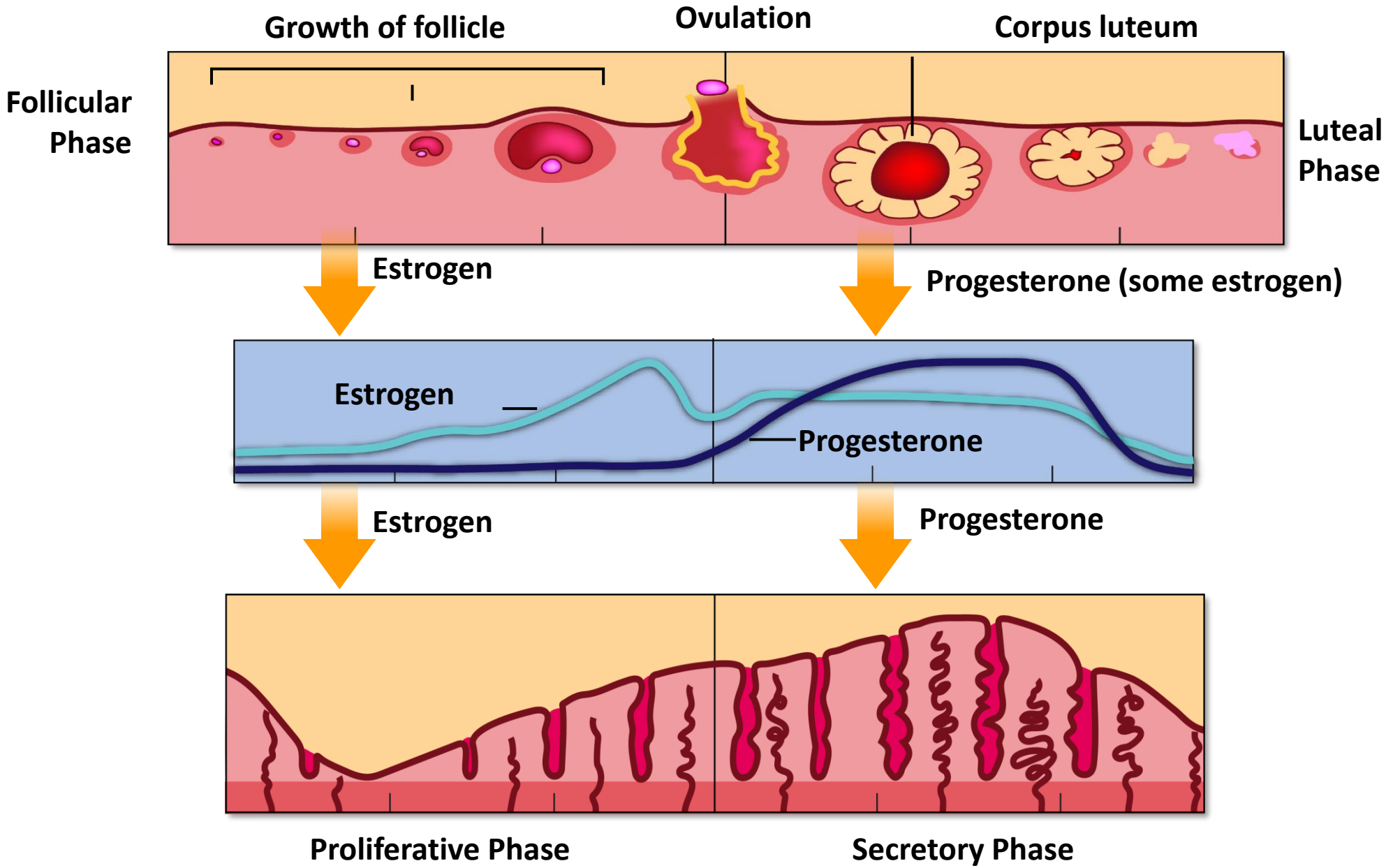
Straw


FMP
Reproductive Phase
Menopausal Transition
Post Menopausal
1 Y R
Perimenopause

Straw


FMP
51.4 years old average age
Reproductive Phase
Menopausal Transition
Post Menopausal
1 Y R
Early Stage-2
Late Stage-1
Average age
47 y.o.
49 y.o.
Perimenopause


80
70
60
50
200
40
160
30
120
20
80
10
40
0
0
FSH
LH
Estradiol
Estrone
44
46
48
50
52
54
56
58
Age (years)


Growth of follicle
Ovulation
Corpus luteum
Follicular Phase
Luteal Phase
Estrogen
Progesterone (some estrogen)
Estrogen
Progesterone
Estrogen
Progesterone
Proliferative Phase
Secretory Phase

Uterine Endometrium

Hormonal status effects endometrial thickness

Endometrium consists of a basalis and functionalis

Estrogen causes the functionalis to proliferate

Progesterone will convert an estrogen-primed endometrial functionalis to a secretory phase

After shedding the functionalis, the basalis endometrium that remains is thin

No estrogenic stimulation of functionalis in menopause

Causes of Menopause

- **Natural menopause**
  - Depletion of eggs in the ovaries
    - No longer at risk of pregnancy
  - Loss of estrogen production from the ovary
  - 50% reduction in testosterone production
  - Biochemical markers of menopause
    - FSH elevated, estrogen reduced
- **Induced menopause**
  - Surgical removal of the ovaries
  - Ovarian failure due to drugs or radiation therapy

Causes of Menopause

Premature menopause: ovarian failure before 40

- Premature ovarian failure (Primary ovarian insufficiency)
  - Autoimmune condition; follicles present
- Resistant ovary syndrome
  - Follicles depleted early; not autoimmune
- Gonadal dysgenesis
  - Fragile X syndrome or mosaic (e.g. 46 xx/xo)

Describe

Describe most common symptoms of perimenopause and menopause

Effects of Menopausal Estrogen Deficiency

- Vasomotor symptoms (VMS)
- Infertility
- Neuro-behavioral changes
- Bone loss
- Genitourinary syndrome of menopause (GSM)
- Acceleration of ASCVD → an increased risk of heart attack, stroke (compared to premenopause)

Vasomotor Symptoms (VMS)

- VMS due to inappropriate triggering of the cooling mechanism
  - Blood vessel dilation + sweating
- Hot flushes (aka: hot flash)
  - Sudden sense of intense body heat
    - Start in the trunk → neck → face
    - Flash perceived before changes can be measured
  - Skin flush (redness of face due to vessel dilation)
- Profuse perspiration follows in the same area
- Seconds to several minutes; up to 20-30 minutes
- Worse at night, but may occur at any time

VMS Mimics:

- Anxiety disorders
- Alcohol, spicy food, food additives (MSG, sulfites)
- Thyroid hormone excess
- Opioid use or withdrawal
- Chronic infection, TB
- Post-gastric surgery dumping syndrome
- Mastocytosis and mast cell disorders
- Pheochromocytoma (hypertension, flushing, sweating)
- Carcinoid syndrome (flushing without sweating)
- Lymphoma, thyroid, pancreatic, renal cell CA
- Medications
  - SSRIs
  - Nicotinic acid (intense warmth, itching up to 30 min)
  - Calcium channel blockers
  - GnRH analogues (e.g., leuprolide)
  - Medications that block estrogen receptors (SERMS like tamoxifen and aromatase inhibitors like letrozole)

Vasomotor Symptoms (VMS)

- Experienced by 75% percent of menopausal women
  - May start during the peri-menopause
  - Cluster in 2-year window before and after FMP
  - 25% have hot flushes > 5 years after menopause
- Smoking and obesity are risk factors
- Ethnic and racial differences
  - More common in African-American women (46%)
  - Less common in Chinese (21%), Japanese (18%)

Duration of Menopausal VMS over the Menopause Transition

- VMS Duration
  - Median =7.4 years
  - Median post-FMP persistence=4.5 years
  - Postmenopausal at the onset of VMS had the shortest median=3.4 years)
  - Premenopausal/early perimenopausal at first symptom, increased duration to 11.8 years, median total VMS duration, and post-FMP persistence median to 9.4 years
  - African Americans had the longest VMS duration (median, 10.1 years)
- Factors related to VMS duration or persistence
  - Younger age
  - Lower educational level
  - Greater perceived stress and symptom sensitivity
  - Higher depressive symptoms and anxiety at first report

Avis NE, et. al, for SWAN. JAMA Int Med.

Neuro-behavioral Changes

- Restful sleep disturbances
- Irritability, fatigue, poor concentration
- Emotional swings; anxiety
  - But depression is *not* related to estrogen deficiency
- Changes in sex drive

Difficult to separate psychological effects due to estrogen deficiency, aging, social changes, and poor sleep

Genitourinary Syndrome of Menopause (GSM)

- Bladder and urethra changes
  - Urgency, frequency, dysuria, urge incontinence
  - Often misdiagnosed as a bladder infection; tests negative
  - No effect on stress incontinence or pelvic organ prolapse
- Vaginal changes
  - Vaginal spotting or bleeding
  - Vaginal dryness
  - Dyspareunia: poor lubrication, less vaginal elasticity, skin irritation, introital shrinkage

Bone Loss and Fracture Risk

- Low estrogen causes loss of calcium from bone
  - Decreased GI absorption of calcium
  - Increased bone resorption (formation same)
- 75% bone loss 15 yrs post-MP due to estrogen deficiency
- “Dowager’s Hump” results from vertebral fractures
- 20% menopausal women will have a hip fracture
  - One-sixth are fatal within 3 months
  - 25% of women with hip fractures require long-term care

Perimenopause: Estrogen's Storm Season

Hormonal changes

- Follicle phase E2 levels can be 20-30% higher
  - Greater variance: higher highs, lower lows
- Luteal phase progesterone peaks are lower

Cycle changes

- Follicle phase shorter (cycle interval now 24-26 days)
- Cycle intervals are less predictable

Bleeding changes

- Flow can be heavier, longer because of more endometrial proliferation (↑E), less endometrial maturation (↓P)

Any 3 Define the Onset of Perimenopause

- New heavy or longer flow
- Shorter menstrual cycle lengths (<25 days)
- New breast tenderness or FCC
- 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, BC Med Journal 2005; 47:534

Support

Support patient-centered approach to management of menopause and perimenopausal symptoms

Contraceptive needs change over the course of one's lifetime

Discuss the patient's concerns about perimenopausal symptoms and offer treatment if desired

Contraceptive Needs, Risks & Benefits Change With Age

- Likelihood of pregnancy decreases with age
- Ovulation is seen in 87.5% of cycles up to 5 years before menopause and 22.8% within 1 year of final menstrual period
- The chance of a naturally occurring pregnancy is 30%/year aged 40-44 and decreases 10% per year from aged 45-49 (rare after 50)
- More than 50% of pregnancies btw 40-44 end in miscarriage, increasing to more than 90% over age 45

Santoro JAMA 2017; Chandra et al., Natl Health Stat Rep, 2013. Avis et al, Monopause 2009; Steiner Fertil Steril 2016.

Choices of Methods in Perimenopause

- No contraceptive method is contraindicated based on age, although medical conditions change over time
- Individualized counseling means you help the patient think about:
  - Baseline health risk for adverse clinical outcomes
  - Menopause-related symptoms of peri-menopause
  - Individual life circumstances and goals
  - Non-contraceptive benefits of the method
  - Some of the features of the contraceptive methods benefit those individuals in the later reproductive years

Combined Hormonal Contraception

Benefits during Perimenopause:

- Pregnancy prevention
- Treatment of vasomotor symptoms / hot flashes
- Predictable menstrual bleeding patterns
- Decreased menstrual blood loss
- Partial protection against bone loss
- Reduced risk of several cancers (especially endometrial and ovarian cancer)

Note: Numerous category 4 MEC conditions and category 3 increase in this age group

Note: When CHC discontinued, menopausal symptoms may start

Combined Hormonal Contraception

- Continuous or extended cycle use may achieve amenorrhea and avoid development of vasomotor symptoms by avoiding hormone-free intervals
- Can use 24/4 regimen
- CHCs with 17-beta-estradiol have less procoagulant effect than COCs with ethinyl estradiol
- Vaginal ring increases vaginal lubrication and may help relieve perimenopausal vaginal dryness and dyspareunia

Subdermal Implants

- Lack estrogen and have few contraindications
- Progestin provides endometrial protections against risks of unopposed estrogen
- Implants cause changes in bleeding patterns in more than 50% of users which can confuse AUB caused by implant use vs. endometrial pathology
- No detrimental effect on bone density
- Theoretically provides adequate endometrial protection when estrogen therapy is used to treat perimenopausal symptoms (off-label use)

Ali et al, 2016; Moray et al, 2021; Hadji et al, 2019

Levonorgestrel Intrauterine Device (LNG-IUD)

- Progestin acts directly on the endometrial lining, causing thinning and glandular atrophy.
- IUD LNG 52 mg is effective for the treatment of patients with endometrial hyperplasia
- LNG-IUD causes amenorrhea
- Over 100 countries have approved LNG 52 mg IUD as progestin for those with an intact uterus using estrogen therapy for menopausal symptoms
- Smoother transition into menopause, helping to avoid AUB that affects many and disrupts quality of life
- Can use as a segue into menopausal hormone therapy

Lethaby et al, 2015; Pal et al, 2018; Joo et al 2021; Bednarek & Jensen 2010

Copper Intrauterine Device (CU-IUD)

- Can increase menstrual blood loss so may not be suitable in the setting of AUB or heavy uterine bleeding in perimenopause
- May be effective far beyond the approved duration of use, so can consider retaining Cu-IUD until menopause, if placed when the IUD user was 35 or older
- Removal is advised once menopause is confirmed
- Cu-IUD associated with decreased risk of endometrial and possibly cervical cancer

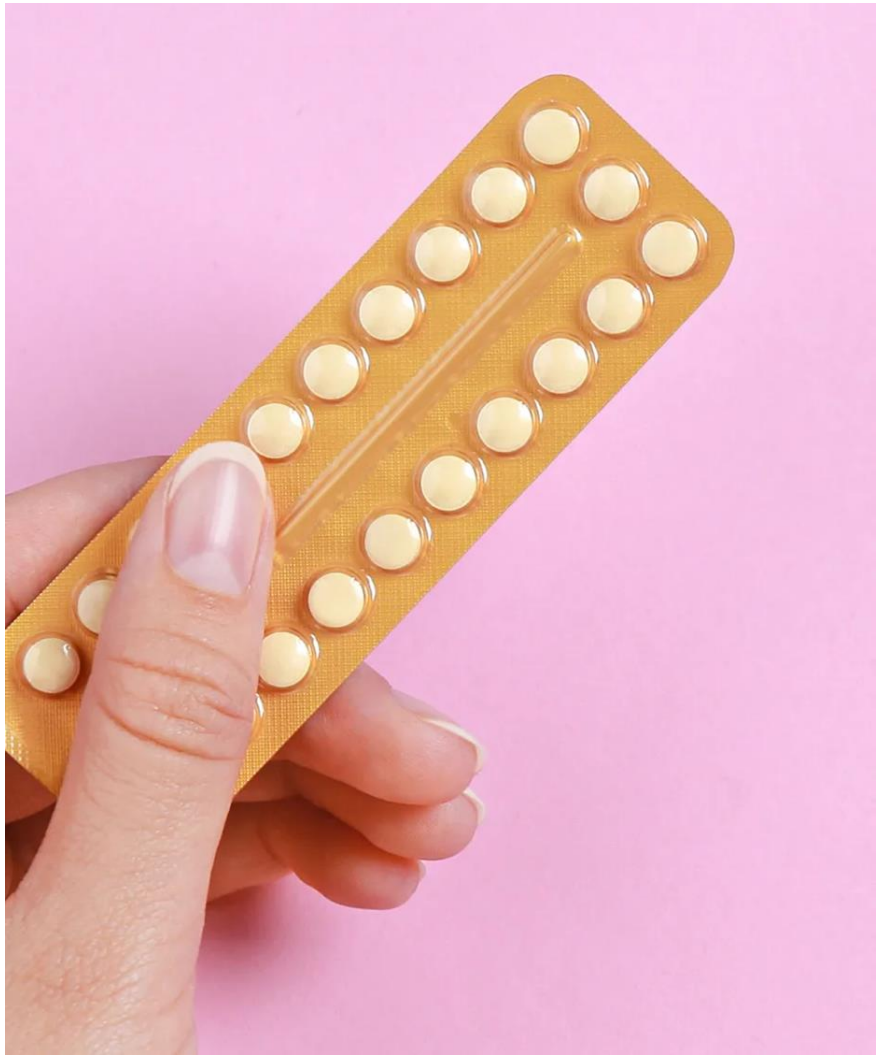
Wu et al., 2014; Ronnerdag et al., 1999; Sivin et al., 1991; Felix et al., 2015; Castellsague et al., 2011

Injectable Progestins: DMPA-IM and DMPA-SC

- Successful treatment of heavy menstrual bleeding is less likely with DMPA compared to the LNG-IUD
- DMPA do not experience accelerated loss in bone density in the first 5 years of menopause
- Past age 50, DMPA continuation should be individualized and weighted against potential risk factors for osteoporosis
- DMPA use is associated with a reduced risk of endometrial hyperplasia and endometrial cancer
- DMPA can be combined with menopausal estrogen therapy to control vasomotor symptoms, off-label
- Does NOT stop FSH level rise in menopause

Hubacher et al., 2009; Kucuk et al., 2008; Harmon et al., 2015; Abdel-Aleem et al., 2013; Cundy et al., 2022; Beksinka et al., 2005

Progestin-Only Pills



- Concurrent breast cancer is listed as the only category condition by the US MEC
- Great to transition from longer-acting methods that induce amenorrhea
- POPs reduce blood loss
- POPs can help reduce vasomotor symptoms
- Not all pills provide predictable scheduled bleeding (drosperinon-only pills have more scheduled bleeding compared to norethindrone-only pills)
- Does NOT suppress menopausal rise in FSH levels

Barrier/Nonhormonal Methods (FABM)

- Symptothermal and 2-day methods have some effectiveness during years of transition
- Decreased fecundity in perimenopause makes less effective methods like diaphragms and cervical caps more acceptable for some patients
- Diaphragms and cervical caps difficult for those with vaginal vault prolapse or significant urethral hypermobility

When can Contraception be Reliably Stopped?

- Confirmation of menopause:
  - Amenorrhea for more than 1 year after age 50
  - Amenorrhea for two or more years if less than 50 years of age
  - FSH greater than or equal to 30 IU/L on two separate occasions, 6-8 weeks apart
    - Can stop DMPA if checked on the day of injection and 13 weeks later at the next injection. If both FSH > 30 IU/L, contraception can be stopped
    - FSH is NOT affected by POPs or implants. If FSH >30, continue for 1 year and then stop. If <30, recheck in one year
    - FSH levels MAY BE affected by use of CHC. Due to a false negative FSH after 7 hormone-free days, FSH levels should be drawn when off CHCs for 2 weeks (preferably 6 weeks). If elevated on two occasions, 6-8 weeks apart, it can stop
- Careful counseling about when to stop using contraception and transitioning to hormonal therapy if desired

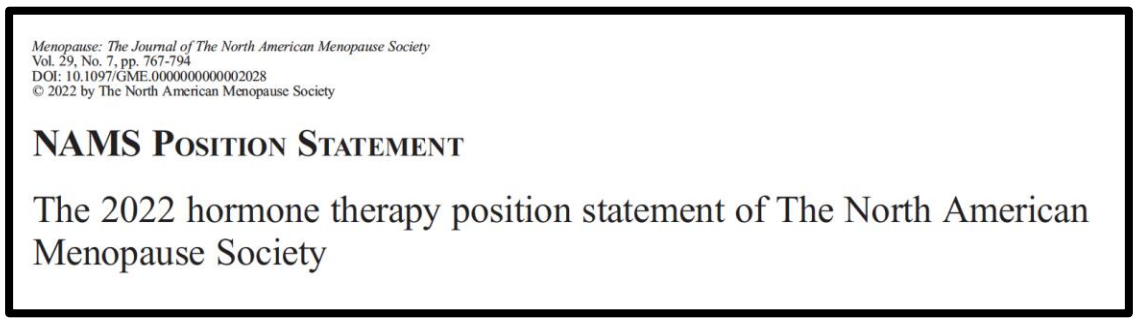
Discuss perimenopausal symptoms and offer treatment

Effects of Menopausal Estrogen Deficiency:

- Vasomotor symptoms (VMS)
- Infertility
- Neuro-behavioral changes
- Bone loss
- Genitourinary syndrome of menopause (GSM)
- Acceleration of ASCVD → an increased risk of heart attack, stroke (compared to premenopause)

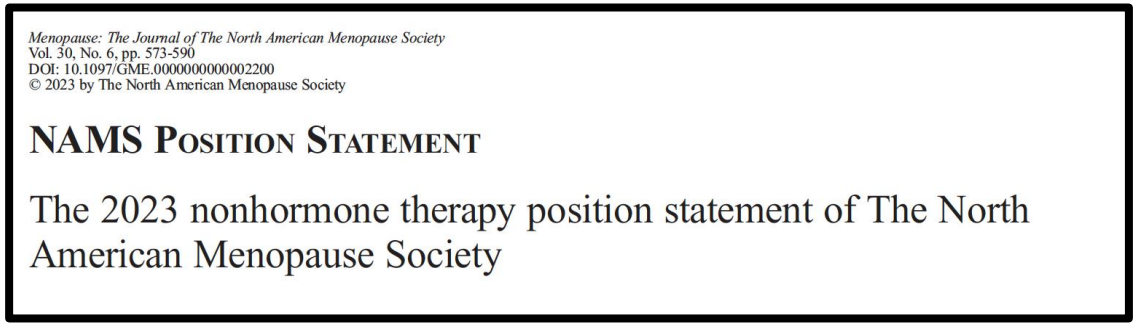
Treatment of Vasomotor Symptoms

NAMS Position Statements


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

NAMS Position Statement

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


Menopause: The Journal of The North American Menopause Society
Vol. 30, No. 6, pp. 573-590
DOI: 10.1097/GME.0000000000002200

NAMS Position Statement

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

Level I: Good and consistent scientific evidence.
Level II: Limited or inconsistent scientific evidence.
Level III: Consensus and expert opinion.

NAMS Definitions

Acronym	Full name
ET	Estrogen (E) therapy
EPT	Combined E+P therapy
HT MHT	Hormone therapy (ET, EPT) Menopausal hormone therapy
P	Progestogen (progesterone or progestin)
CC-EPT	Continuous-combined E+P therapy
CS-EPT	Continuous-sequential E+P therapy

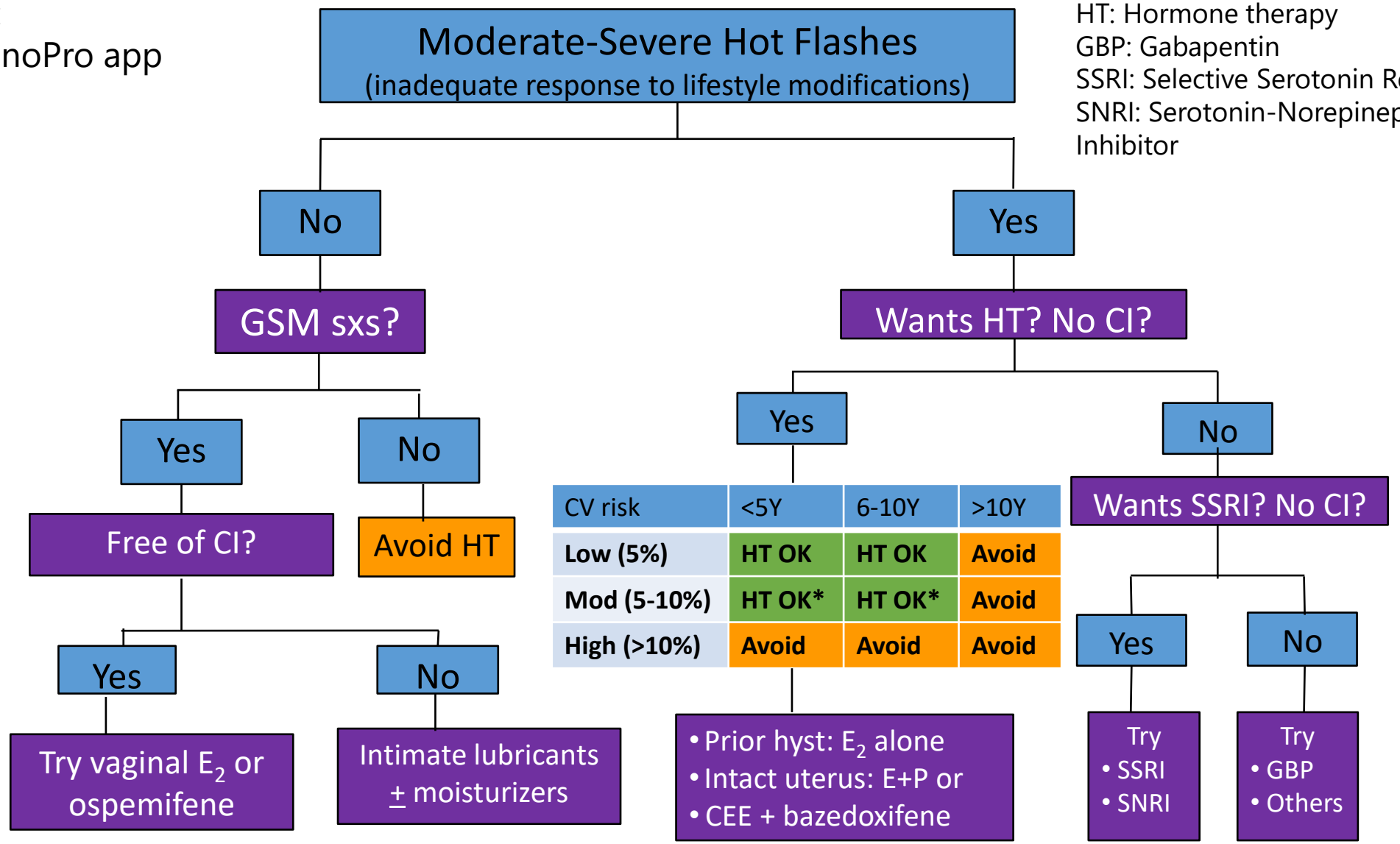
NAMS
The North American Menopause Society

NAMS Definitions

Abbrev[n]	Definition
VMS	Vasomotor Symptoms
VVA	Vulvovaginal Atrophy
GSM	Genitourinary syndrome of menopause
T	Testosterone
SHBG	Sex hormone binding globulin

Reference:
NAMS MenoPro app

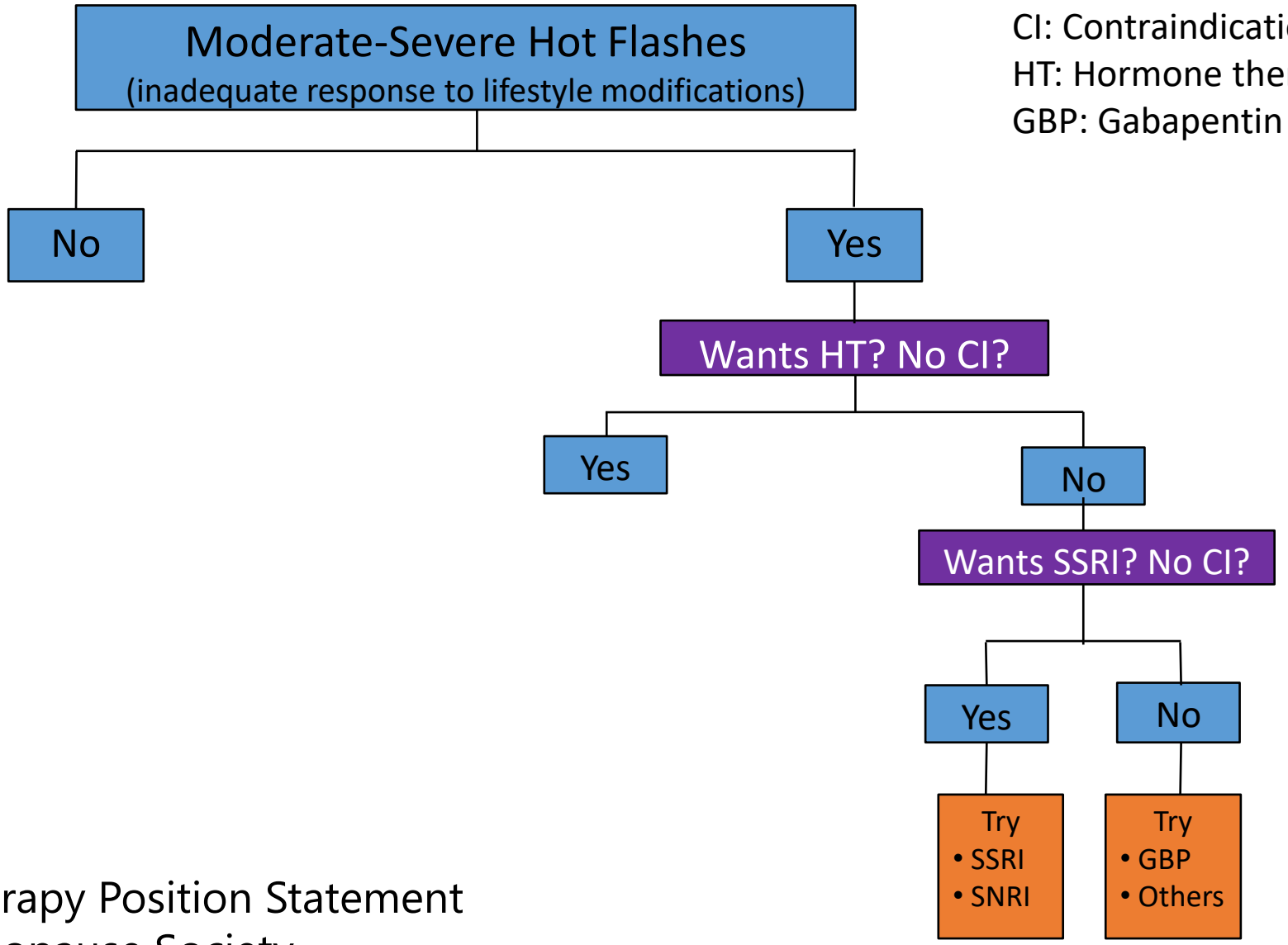
CEE: Conjugated equine estrogen
CI: Contraindication
HT: Hormone therapy
GBP: Gabapentin
SSRI: Selective Serotonin Reuptake Inhibitor
SNRI: Serotonin-Norepinephrine Reuptake Inhibitor



* Consider transdermal hormone therapy

Case Study 1: Dolores

- 48-year-old female
- Cycles are 27-35 days apart
- C/o mild-moderate hot flashes, especially at night
- Occasionally feels depressed, but not treated
- Non-smoker; no medications; generally healthy
- PE: BP 122/78, BMI 26 kg/m^2
- Would like treatment for hot flashes, but “scared of hormones”



CI: Contraindication
HT: Hormone therapy
GBP: Gabapentin

Reference:
The 2023 Nonhormone Therapy Position Statement of the North American Menopause Society.
Menopause 2023; 30(6): 573-590

VMS Recommended Therapies

Options:

- FDA-approved low-dose paroxetine salt
- Other SSRIs and SNRIs yield significant VMS reductions in large RCTs
- Gabapentin
- Fezolinetant
- CBT (cognitive behavioral therapy)
- Clinical hypnosis
- Oxybutynin (Levels I-II)
- Weight loss (Levels II-III)
- Stellate ganglion block (Levels II-III)

Choice of medication depends on:

- Patient preference
- Coexistence of mood disorder
- VMS more bothersome day or night
- Medication sensitivity
- Pharmacogenetic testing

NAMS
The North American Menopause Society

VMS: Non-Hormonal Therapies

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

J Clinical Oncology 2009

Prescription Therapies: Considerations

- Start lowest dose
  - Titrate up to effect, tolerance
  - Onset of action usually w/in 2 weeks
- When stopping, taper therapy over 1-2 weeks
- Re-evaluate carefully and regularly Q 6-12 months
- Available formulary options

NAMS
The North American Menopause Society

Dosing Ranges for Nonhormonal Drugs

Drug	Brand name	Range (mg/day)	Comment
Paroxetine salt	Brisdelle	7.5mg	Single dose, no titration needed
Paroxetine	Paxil	10-25	Start with 10 mg/d
Citalopram	Celexa	10-20	Start with 10 mg/d
Escitalopram	Lexapro	10-20	Start with 10 mg/d (for sensitive or older persons, start 5 mg/d
Desvenlafaxine	Pristiq	100-150	Start with 25-50 mg/d and titrate up by that amount each day
Venlafaxine	Effexor	37.5-150	Start with 37.5 mg/d
Gabapentin	Neurontin	900-2,400	300mg at night, then add 300 mg at night, then a separate dose of 300mg in the morning
Fezolinetant	Veozah	45mg	Single dose, no titration needed

VMS: Do Not Recommend

- Paced respiration (level I)
- Over-the-counter supplements, Herbal therapies, Vitamins (level I-II)

Level II:

- Cooling techniques
- Avoiding triggers
- Exercise
- Yoga
- Mindfulness-based intervention
- Relaxation
- Soy and soy extracts, soy metabolite equol
- Cannabinoids
- Suvorexant
- Acupuncture
- Calibration of neural oscillation

NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

VMS: Do Not Recommend

Level III evidence:

- Chiropractic intervention
- Clonodine
- Dietary modification
- Pregabalin

NAMS *Menopause*. 2015;22(11):1155-74

NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

Options for Dolores

- Given mild depression, offer paroxetine 10 mg QD
  - Titrate upward, as needed, for hot flashes and depression
- If not, offer venlafaxine 37.5 mg, then titrate up
- If not, offer gabapentin 300mg at night, then titrate up
- If Rx medications are not acceptable, discuss “supplements” with black cohosh (e.g., Estroven and others)
  - Slightly better improvement than placebo
  - Duration of improvement usually < 6 months
  - Few side effects

Case Study 2: Nicki

- 46-year-old G_2 P_2 female seen with a c/o of hot flashes and irregular menstrual cycles for 2 years
  - Menstrual interval “3 weeks up to 3 months”
  - Bleeding is heavy for first 3 days
  - No intermenstrual bleeding
  - Has premenstrual molimina
- Sexually active, not using contraception
- Healthy; no cardiovascular risk factors

Hormonal Contraceptives in Perimenopause

- OCs (< 30 mcg EE) provide relief VMS *and* pregnancy prevention
  - Other benefits: cycle control, fewer ovarian cancers
  - Patch or ring may be helpful, but no studies on VMS relief
- LNg-IUD prevents endometrial hyperplasia when used with ET
  - But…LNg-IUD and DMPA alone will not address VMS
- Decision to discontinue contraception is based on balance of possible adverse effects vs. pregnancy risk with waning fertility
  - Highly individualized on both counts

NAMS
The North American Menopause Society

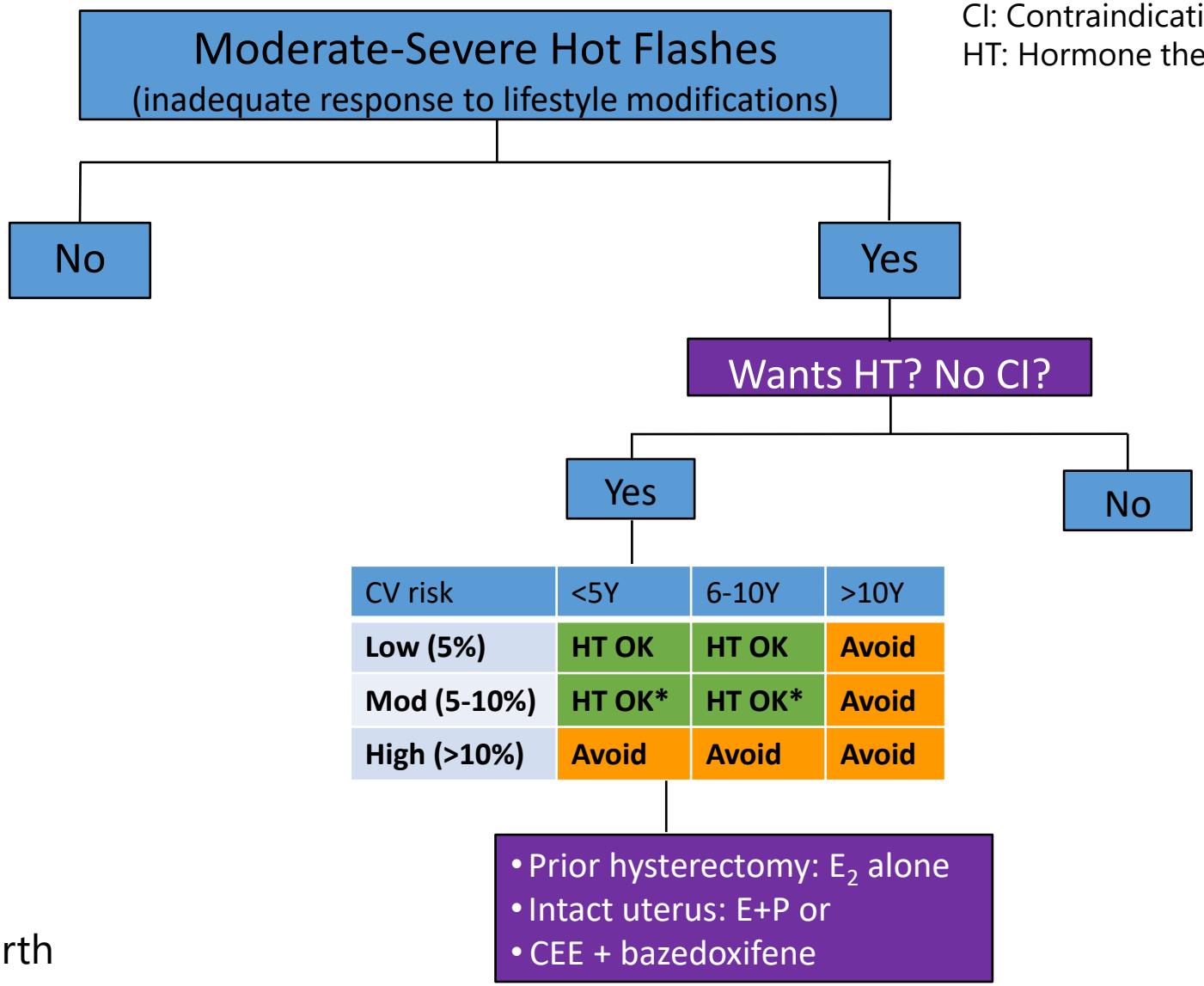
Options for Nicki

- Oral contraceptive (20 mcg ethinyl estradiol) aiming for
  - Hot flash improvement
  - Pregnancy prevention
  - Cycle regularity (or amenorrhea if used continuously)
- Contraceptive vaginal ring, used continuously
- Contraceptive patch (cycle 21 days on, 7 days off)
- Progestin-only methods will control irregular bleeding and prevent pregnancy only, but no effect of hot flashes

Case Study 3: Sara

- 53-year-old female with moderate-severe hot flashes and difficulty getting to sleep
- Menses were regular until one year ago, became irregular, and then stopped 16 months ago
- Tried herbal remedies…each helped for a few months
- Medical history, BP, physical exam are normal
- Flashes affect work productivity; wants something stronger

E: estrogen
P: progestagen
CI: Contraindication
HT: Hormone therapy



Reference:
The 2022 Hormone Therapy Position Statement of the North American Menopause Society.
Menopause 2022; 29 (7):767-794

* Consider transdermal hormone therapy

NAMS Recommendations For Clinical Care

- Menopausal hormone therapy is the most effective treatment for vasomotor symptoms
- Options include
  - Estrogen alone
  - Estrogen-progestogen
  - Estrogen-bazedoxifene
  - Progestogen alone, or
  - Combined OCs in persons requiring contraception

NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

Prescription HT Options: ET and EPT

	Oral	Transdermal	Intravaginal
ET	• Micronized estradiol • Conjugated equine estrogens (CEE) • Synthetic conjugated estrogens • Esterified estrogens • Estropipate • Estradiol acetate	• Patches • Gels • Emulsion • Spray	• Creams • Intravaginal tablet • Rings
EPT	• CC-EPT • CS-EPT	• E+P combination patches	

HT: Routes of Administration

- No clear benefit of one route of administration
- Transdermal ET has lower DVT/PE risk than oral ET
- Local ET preferred when solely vaginal symptoms
- With either route, progestogen required for endometrial protection from unopposed estrogen

NAMS Position Statements

NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

"First Line" Use: Transdermal Estrogen

- Underlying medical conditions
  - History of DVT or PTE
  - High triglyceride levels
- Need for "steady state" drug release
  - Daily mood swings (especially while on oral HT)
  - Migraine headaches
- Inability to use oral tablets
  - Stomach upset due to oral estrogen intake
  - Problems with taking a daily pill

Hormone Therapy Dosages

- Therapeutic goal is lowest effective estrogen dose (plus low dose P) c/w goals, benefits, risks
  - Lower doses better tolerated, may have more favorable benefit-risk ratio than standard doses
- Local ET may be needed for persistent GSM symptoms
- Lower doses may take 6-8 weeks to provide relief

NAMS
The North American Menopause Society

HT *Starting* Dosages

Typical *lowest* doses of estrogen

- 0.5 mg oral micronized 17ß-estradiol
- 0.3 mg oral conjugated estrogen (CE)
- 0.014-0.025 mg transdermal 17ß-estradiol patch

Typical *lowest* doses of progestogen

- 1.5 mg oral MPA
- 0.1 mg oral norethindrone acetate
- 0.5 mg oral drospirenone
- 50-100 mg oral micronized progesterone

HT *Standard* Dosages

Estrogen

- 1.0 mg oral micronized 17ß-estradiol
- 0.625 mg oral conjugated estrogen (CE)
- 0.0375-0.050 mg transdermal 17ß-estradiol patch

Progestogen

- 2.5 mg oral MPA (CC) or 5.0 mg MPA (CS)
- 100 mg oral micronized progesterone (CC) or 200 mg PO at bedtime (CS)

NAMS Position Statement, Menopause. 2010; 17(2):242-55

NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

HT: Adjusting Estrogen Dosage

- Start *low dose* transdermal or oral estrogen
- If suboptimal response, modify by…
  - Change the estrogen dose (upward)
  - Change the estrogen preparation
  - Change delivery systems (oral ⇄ transdermal)
  - Consider an estrogen + androgen (Covaryx)
- Injectable estrogen not recommended
  - Dosage equivalencies are not known
  - Estrogen cannot be discontinued easily

Progestin-Only Therapy Dosages

- P-alone may be used to treat hot flashes, but is not as effective as ET or EPT regimens
- P formulations effective in treating VMS (per day)
  - MPA 10 mg
  - Megestrol acetate 20 mg
  - Micronized progesterone 300 mg
- No long-term studies have addressed the safety of P-only treatment on menopause symptoms

Options for Sara

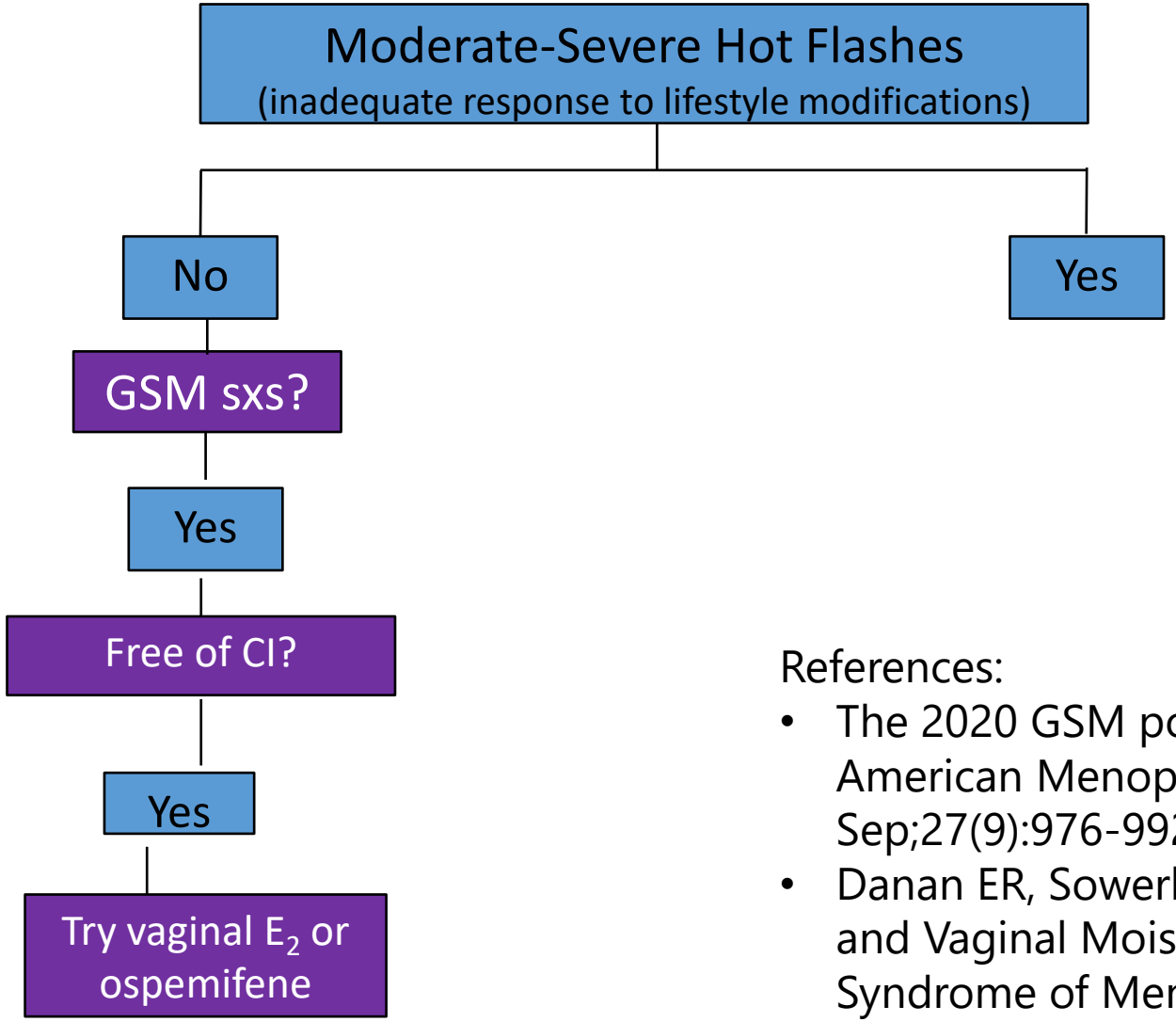
- Offer continuous combined HT:
  - Micronized estradiol 0.5 mg QD *or* 17-b estradiol patch 0.025 mg twice weekly, and…
  - Medroxyprogesterone acetate (MPA) 2.5 mg QD *or* micronized progesterone 100 mg PO at bedtime
- If she prefers single dose daily product, offer:
  - Combination estrogen + progestin patch
  - Combination estrogen + progestin tablet
  - Bazedoxifene 10 mg + conjugated estrogen 0.45 mg

Case Study 4: Betty

- 53-year-old G_4 P_3 female with vulvovaginal dryness and irritation
- Menopause 2 years ago; no history of post-menopausal bleeding
- Sexually active “one or twice a week”, but reports that sex is quite uncomfortable
- Intermittently uses water-based lubricant
- No complaint of hot flashes or sleep problems

Genitourinary Syndrome of Menopause (GSM)

- Vaginal changes
  - Vaginal spotting or bleeding; dryness
- Dyspareunia: poor lubrication, less vaginal elasticity, skin irritation, introital shrinkage
  - Negative impact on relationship(s), quality of life
- Bladder and urethra changes
  - Urgency, frequency, dysuria, urge incontinence
  - Often misdiagnosed as bladder infection; tests negative
  - No effect on stress incontinence or pelvic organ prolapse



CI: Contraindication
HT: Hormone therapy
E_2: estradiol

References:

- The 2020 GSM position statement of the North American Menopause Society. Menopause. 2020 Sep;27(9):976-992
- Danan ER, Sowerby C, et.al. Hormonal Treatments and Vaginal Moisturizers for Genitourinary Syndrome of Menopause : A Systematic Review. Ann Intern Med. 2024 Oct;177(10):1400-1414

GSM Treatment

- Lubricants often improve vaginal dryness and painful sex
- When HT is considered solely for this indication, vaginal estrogen is recommended
- Progestogen *not indicated* with low-dose, local vaginal estrogen

NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

GSM: Treatment

- OTC lubricants
  - Water based: Astroglide®, KY Jelly®, Sliquid®
  - Silicone based: K-Y intrigue®, Astroglide X®
  - Oil based: Elegance®, olive oil, coconut oil
- Vaginal moisturizers: Luvena®, Vagisil®, Replens®
- Local estrogen therapy
  - Cream, vaginal tablet, vaginal ring
- Systemic HT (when prescribed for VMS)
- Oral ospemifene (SERM)
- Intravaginal DHEA

Topical (Vaginal) Estrogen

Composition	Brand Name	Dose and sig
Vaginal cream 17β-Estradiol	Estrace® Vaginal Cream	Initial: 2.0-4.0g/d for 1-2 wk. Maint: 1.0g/d (0.1 mg/g)
Vaginal cream conj estrogens	Premarin® Vaginal Cream	0.5-2.0 g/d or twice/wk (0.625 mg/g)
Vaginal ring 17β-estradiol	Estring®	Ring contains 2 mg releases 7.5 mcg/d for 90 d
Vaginal ring E_2 acetate	Femring® (Systemic dose and indication)	Systemic dose ring for 90 d 12.4mg releases 50mcg/d 24.8mg releases 100mcg/d
Vaginal tablet E_2 hemihydrate	Vagifem® 10mcg	Initial: 1 tablet/d for 2 wk Maintenance: 1 tab 2x /wk
Estradiol vaginal insert	Imvexxy® 4 mcg and 10 mcg	Initial: 1 tablet/d for 2 wk Maintenance: 1 tab 2x /wk

NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

Options for Betty

- Use water-based or silicone based intimate lubricant with all sexual encounters
- Offer (formulary) topical vaginal estrogen cream or tablet
- Offer (formulary) estrogen-releasing vaginal ring
- Offer ospemifene PO
- Offer DHEA (prasterone) vaginal insert

Free | Confidential | Nationwide

Reproductive Health Hotline

ReproHH

UCSF
University of California
San Francisco

For Clinicians By Clinicians

844-ReproHH

844-737-7644

Monday-Friday
8 am-4pm PT

Experts in sexual and reproductive health available on-demand to answer your questions!

Contraception | Miscarriage | Abortion | Pregnancy | Vaginitis
STIs | Gynecologic procedures and pain management | Menopause
Abnormal Uterine Bleeding | And More!

Learn more & review our terms of service at ReproHH.ucsf.edu

Download our contact information by scanning our v.card here

“Aging is not lost youth but a new stage of opportunity and strength.” - Betty Friedan

“Women over 50? We’re just getting started!” -Chaka Khan

Additional Resources:

Ovary Active: A podcast for your patients with questions about perimenopause and menopause: https://podcasts.apple.com/us/podcast/ovaryactive/id1771890856

The Menopause Society: https://menopause.org/

General References

- Avis NE, et. al, Duration of Menopausal Vasomotor Symptoms Over the Menopause Transition. JAMA Intern Med 2015; 175(4):531-539
- Cobin R, Goodman N; American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on Menopause-2017 Update. Endocr Pract. 2017; 23(7):869-880.
- Crandall CJ, Mehta JM, Manson JE. Management of Menopausal Symptoms: A Review. JAMA 2023; 329(5):405-420
- Delamater L, Santoro N. Management of the Perimenopause. Clin Obstet Gynecol. 2018 Sep;61(3):419-432
- de Villiers TJ, Gass ML, Haines CJ, et.al. Global consensus statement on menopausal hormone therapy. Climacteric. 2013; 16(2):203-4
- Faubion SS, Sood R, Kapoor E. Genitourinary Syndrome of Menopause: Management Strategies for the Clinician. Mayo Clin Proc. 2017 Dec;92(12):1842-1849
- Hill DA, Crider M, et al. Hormone Therapy and Other Treatments for Symptoms of Menopause. Am Fam Physician. 2016; 94:884-889
- Phillips NA, Bachmann GA. Genitourinary syndrome of menopause: Common problem, effective treatments. Cleve Clin J Med. 2018; 85(5):390-39

General References

- Kaunitz AM, Manson JE. Management of Menopausal Symptoms. Obstet Gynecol. 2015 Oct;126(4):859-76
- Marjoribanks J, Farquhar C, et.al. Long-term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev. Jan 2017
- McNeil MA, Merriam SB. Menopause. Ann Intern Med. 2021 Jul;174(7):ITC97-ITC112
- Santoro N, Epperson CN, Mathews SB. Menopausal Symptoms and Their Management. Endocrinol Metab Clin North Am. 2015 Sep;44(3):497-515
- Santen RJ, Stuenkel CA, Davis SR, et.al. Managing Menopausal Symptoms and Associated Clinical Issues in Breast Cancer Survivors. J Clin Endocrinol Metab. 2017; 102(10):3647-366
- Shufelt C, Manson J. Managing Menopause by Combining Evidence With Clinical Judgment. Clin Obstet Gynecol 2018; 61(3):470-479

NAMS References

- NAMS. The 2023 Nonhormone Therapy Position Statement of the North American Menopause Society. Menopause 2023; 30(6): 573-590
- NAMS: The 2022 Hormone Therapy Position Statement of the North American Menopause Society. Menopause 2022; 29 (7):767-794
- NAMS Statement on Continuing Use of Systemic Hormone Therapy After Age 65. Menopause 2015; 22(7): 693
- Kaunitz AM, Manson JE. Failure to treat menopausal symptoms: a disconnect between clinical practice and scientific data. Menopause. 2015 Jul;22(7):687-8
- Manson JE, Ames JM, et al. Algorithm and mobile app for menopausal symptom management and hormonal/non-hormonal therapy decision making: a clinical decision-support tool from NAMS. Menopause. 2015 Mar;22(3):247-53
- Pinkerton JV. Hormone Therapy: Key Points From NAMS 2017 Position Statement. Clin Obstet Gynecol. 2018;61(3):447-453

Appendix

ET: Oral Tablets

Product	Brand	Standard dose	Low dose
Conjugated equine estrogen (CEE)	Premarin	0.625 mg	0.3, 0.45 mg
Conjugated estrogen (synth)	Cenestin Enjuvia	0.625 mg	0.3, 0.45 mg
Esterified estrogen	Menest Estratab	0.625 mg	0.3 mg

ET: Oral Tablets

Product	Brand	Standard dose	Low dose
Estropipate	Ogen Ortho-est Generic	0.625 mg	none
Micronized E_2	Estrace Generic	1.0 mg	0.5 mg
Estradiol acetate	Femtrace	0.9 mg	0.45 mg

ET Transdermal: Patch*

Brand name	Mg/24 hr	Use/ wk
Alora	0.025, 0.05, 0.075, 0.1	2
Esclim	0.025, 0.0375, 0.05, 0.075, 0.1	2
Estraderm	0.05, 0.1 (reservoir)	2
Vivelle	0.05, 0.1	2
Vivelle-Dot	0.025, 0.0375, 0.05, 0.075, 0.1	2
Climara	0.025, 0.0375,0.05, 0.06, 0.075, 0.1	1
Menostar	0.014 ☼	1

ET Transdermal: Patch*

Patch	Brand	Source	Dose
E_2 matrix	Alora, Climara, Vivelle, Vivelle-Dot, Menostar	Soy/Yams	0.05mg
	E_2 is embedded in the adhesive layer applied directly to the skin		
E_2 reservoir	Estraderm	Soy/Yams	0.05mg
	E_2 release is controlled by a co-polymer membrane; contains more layers than matrix patch		

ET Transdermal: Gels, Emulsions, Sprays*

Brand name	Type	mg/24 hr	Use
Divigel	Gel	0.25, 0.5, 1 mg/ packet	1 packet daily
Elestrin	Gel	0.87 gm pump	1 pump daily
EstroGel	Gel	1.25 gm pump	1 pump daily
Estrasorb	Emulsion	1.74 gm/ pouch	2 pouches daily
Evamist	Spray	1.53 mg/ spray	1 spray daily

* All contain 17B- estradiol only

ET Transdermal: Gels, Emulsions, Sprays*

Transdermal	Brand	Source	Equivalents
E_2 gel No direct comparison trials. Dose equivalents are estimates	Divigel	Soy/Yams, Sunflower seeds, Rapeseed, Poppy seeds, Pine trees	1g packet
	Elestrin	Soy, Rapeseed, Pine tree wood	2-3 pumps
	Estrogel	Oil seed, Soy, Pine tree wood	.035mg
E_2 emulsion	Estrasorb	Soy	2 packets
E_2 spray	Evamist	Soy/ Yams	3 sprays

Progesterone/ Progestin Products

Oral Progestin	Equiv dose	Available doses
MPA (Provera®)	5-10 mg	1.2, 2.5, 5, 10 mg
Micronized progesterone (MP) (Prometrium®)	200-300 mg	100, 200 mg
Drospirenone (DRSP)	0.5 mg/d	0.5 mg/d
Norethindrone acetate (NETA)	1.0 mg/d	0.5, 1.0 mg/d
Norethindrone (NOR)	0.7-1.0 mg/d	0.35 mg
Norgestimate (NGM)	0.09 mg	0.09 mg
Norgestrel (LNg)	150 mcg/d	150 mcg/d

EPT: Oral Tablets

Brand name	Estrogen	Progestin	Dosing
Activella	17β-E2 1 mg	NETA 0.5 mg	Once daily oral
Angeliq	17β-E2 1 mg	Drospirenone 0.5 mg	Once daily oral
FemHRT	EE 5 μg EE 2.5 μg	NETA 1 mg NETA 0.5 mg	Once daily oral
Prefest	17β- E2 1 mg	Micronized NGM 0.09 mg	E (alone) 3 days E+P 3 days
Premphase 14 active/14 pbo	CEE 0.625 mg	MPA 5 mg	Once daily oral (CS-EPT)
Prempro 28 active	CEE 0.625 mg 0.45 mg 0.3 mg	MPA 5.0 mg; 2.5 mg 2.5 mg 1.5 mg	Once daily oral (CC-EPT)

EPT: Transdermal Patches

Brand name	Estrogen	Progestin	Dosing
CombiPatch	17β-E2 0.05 mg 0.05 mg	NETA 0.14 0.25 mg	Twice weekly
Climara Pro	17β-E2 0.045 mg	LNg 0.015 mg	Once weekly

Compounded Hormone Therapy

- The *marketing* of compounded hormonal therapy
  - Only bioidentical hormones are used
  - Combination of 2 or 3 estrogens is more “natural”
  - Dosage is tailored to the individual
  - More “pure” than commercial products
  - Safer delivery systems (no dyes, etc)
- *The reality*
  - The *same* hormones are used in commercial and compounded 17b-E_2 and progesterone

Duralde, et al., BMJ 2023;382:e072612 | doi: 10.1136/bmj-2022-072612

Compounded Hormone Therapy

- Compounded bioidentical HT presents safety concerns
  - Minimal government regulation and monitoring
  - Overdosing or under-dosing
  - Presence of impurities or lack of sterility
  - Lack of scientific efficacy and safety data
  - Lack of a label outlining risks
- Salivary hormone testing to for dosing is unreliable
- Prescribers should document the medical indication for compounded HT over FDA-approved therapies

NAMS
The North American Menopause Society

Compounded Hormone Therapy

Compounded hormones probably will work about as well as commercial HT products, but…

- The value of adding E_1 + E_3 has not been evaluated
- Progesterone skin cream is not absorbed
- Compounded hormone doses are not standardized
- Salivary hormone levels are not useful
- FDA-approved HT products will offer
  - Bioidentical hormones
  - Choice of delivery systems
  - Formulary coverage/ lower out-of-pocket costs