

Hormone Therapy Unlocked: Overcoming Barriers to Better Care

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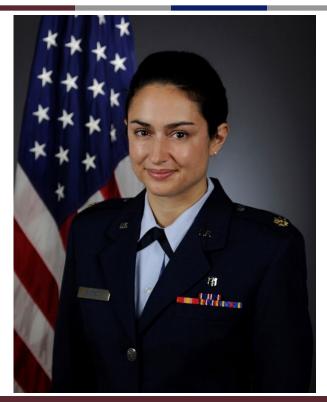
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Air Force Lt. Col. Samantha Simpson, M.D., NCMP



Air Force Lt. Col. Samantha Simpson, M.D., NCMP is the Reproductive Endocrinology and Infertility division director at Brooke Army Medical Center, 959th Surgical Operations Squadron, Joint Base San Antonio – Fort Sam Houston, Texas. She oversees specialty care clinic patients, conducting over 1,200 office visits and 120 in vitro fertilization cycles annually. Lt Col Simpson also serves as the Obstetrics and Gynecology Residency Program Director, with administrative and clinical oversight of 24 obstetrics and gynecology residents. She is a Nationally Certified Menopause Practitioner by the Menopause Society.

Lt Col Simpson holds an Associate Professorship position at the Uniformed Services University of the Health Sciences (USUHS) Center and provides education and clinical teaching to 30 San Antonio Uniformed Services Health Education Consortium interns, 50 USUHS medical students, and her 24 obstetrics and gynecology residents, hoping to make them all advocates for women and clinical experts in perimenopause and menopause management.





Aoife O'Sullivan, M.D., NCMP



Aoife O'Sullivan, M.D., NCMP is a board-certified family medicine and menopause certified practitioner. She is the founder of Portland Menopause Doc, a telemedicine practice. Originally trained in Ireland, she completed a family medicine residency there before moving to the United States in 2004, where she completed a second residency at the University of Maryland. Dr. O'Sullivan has over 30 years of experience and is specialized in the comprehensive care of midlife women. She is passionate about addressing the long-standing gaps in menopause education and care, delivering educational lectures in graduate medical education programs, medical societies and professional organizations, but also to lay businesses and the community throughout Oregon and Washington. An influential voice in the digital health space, Dr. O'Sullivan is active on social media where she empowers women with knowledge and inspires dialogue about midlife health. She is the cohost of the new podcast, "The Dusty Muffins."





Rebbecca Hertel, DO, MSCP



Rebbecca Hertel, DO, MSCP is a board-certified osteopathic family medicine physician and certified menopause practitioner and the founder and CEO of Osteopathic Midlife Health, a telemedicine practice dedicated to midlife and menopause care. With over 20 years of expertise, Dr. Hertel has provided compassionate, patient-centered care across all life stages since completing her residency in 2009. A passionate advocate for women's health, she is committed to advancing education and awareness about the unique changes women experience during perimenopause and menopause. Dr. Hertel regularly teaches medical students, and she educates colleagues to improve understanding and care in family medicine. Beyond her clinical work, she delivers menopause education to providers, students, and communities through lectures, panels and podcasts. Dr. Hertel has a large social media presence on multiple platforms where she shares valuable insights, resources, and support to help women thrive in midlife and beyond. She is the co-host of the podcast, "The Dusty Muffins."





Air Force Col. (ret.) Christine Hart Kress, DNP, APRN, WHNP-BC, NEA-BC, MSCP



Air Force Col. (ret.) Christine Hart Kress, DNP, APRN, WHNP-BC, NEA-BC, MSCP is a board-certified women's health nurse practitioner and certified menopause practitioner. She is the CEO and owner of a specialized telemedicine practice focused on comprehensive menopause and midlife care. Dr. Hart Kress is a seasoned healthcare leader with over 30 years of experience in women's health and 27 years of service in the Air Force as a nurse practitioner and healthcare executive. After retirement, she transitioned to a Chief Nursing Officer role in a hospital system then returned to clinical practice in gynecology. Her passion lies in transforming access to high-quality care for women in midlife and menopause. A published author in the field of women's health, Dr. Hart Kress has a large social media following and has been featured on multiple podcasts and blogs, sharing her expertise and insights. She is the co-host of the new podcast, "The Dusty Muffins." She has received numerous accolades for her clinical excellence and leadership. including the Air Force Medical Service Advanced Practice Nurse of the Year and Tucson's Fabulous 50 Nurses awards.





Heather C. Quaile, DNP, WHNP-BC, MSCP, CSC, I.F., FAANP



Heather C. Quaile, DNP, WHNP-BC, MSCP, CSC, I.F., FAANP is a clinical and academic leader and entrepreneur. She is the founder, Owner and Clinical Director of The SHOW Center, a women's health and sexual medicine practice. Dr. Quaile is a double board-certified, women's health nurse practitioner and advanced forensic nurse specializing in human trafficking and female sexual health, she created and implemented a medical program, the first of its kind emergency stabilization for commercial sexual exploitation of youth in Georgia. Additionally, she is also a certified menopause practitioner, trained and certified as an American Association of Sexuality Educators, Counselors and Therapists (AASECT) sex counselor and sexual assault nurse examiner providing sexual health education. trauma-informed care, and information to patients of all ages. Dr. Quaile has been working in all aspects of women's healthcare for over 23 years caring for women of all ages across the health-illness continuum. Her social media is full of medical education @drquailenp. She is the founder and co-host of the podcast, "justASK."





Disclosures

- Lt Col Simpson, Dr. Hertel, Dr. O'Sullivan, Dr. Hart Kress and Dr. Quaile have no relevant financial or non-financial relationships to disclose relating to the content of this activity.
- The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of Defense, nor the U.S. Government.
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Learning Objectives

At the end of this presentation, participants will be able to:

- 1. **Define menopause and perimenopause**, outlining key hormonal and physiological changes, and identify the clinical presentations and symptoms associated with these transitional stages.
- 2. Analyze the historical context of hormone therapy and midlife care, including the influence of the Women's Health Initiative (WHI) study, and evaluate subsequent research that informs modern, evidence-based approaches to care.
- 3. Identify the clinical presentation of perimenopause and explore evidence-based prescribing strategies and therapeutic options to effectively manage symptoms and improve patient outcomes.
- 4. Apply current clinical guidelines and insights and laboratory studies to prescribe hormone therapy tailored to the individual needs of menopausal patients with confidence and precision, ensuring evidence-based and personalized care.
- 5. Describe the symptoms and underlying causes of Genitourinary Syndrome of Menopause (GSM) and discuss its impact on sexual health, urinary health, and overall quality of life, along with management strategies.





- 1. How confident are you in managing perimenopause-related symptoms (e.g., vasomotor symptoms, sleep disturbances) in female DoD patients?
 - a. Very confident
 - b. Somewhat confident
 - c. Neutral
 - d. Somewhat unconfident
 - e. Very unconfident





- 2. Have you received any formal training specific to managing menopause and sexual health in female patients?
 - a. Yes
 - b. No





- 3. What do you believe are the most significant barriers to managing perimenopause and menopause in military health care settings? (Select all that apply)
 - a. Time constraints
 - b. Stigma associated with sexual health concerns
 - c. Lack of specialized resources
 - d. Limited training on the subject
 - e. Cultural or institutional challenges





- 4. Do you feel equipped to discuss hormonal therapies (e.g., hormone replacement therapy) with female DoD patients experiencing menopause?
 - a. Yes
 - b. No
 - c. Uncertain





- 5. Do you feel that there is a stigma surrounding the discussion of sexual health and menopause in military health care?
 - a. Yes, significant stigma
 - b. Yes, some stigma
 - c. Neutral
 - d. No, minimal stigma
 - e. No, no stigma at all





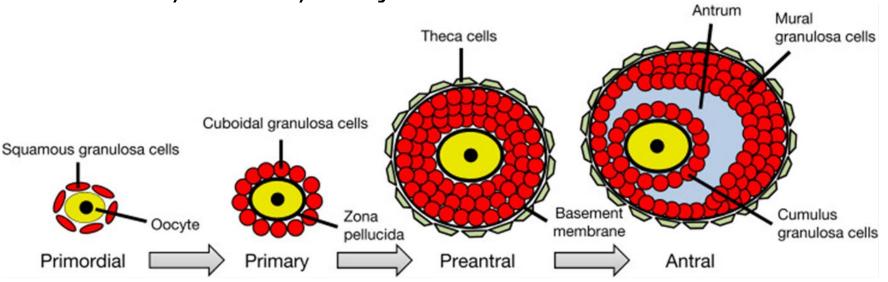
- 6. How often do you refer female patients for specialist care (e.g., gynecology, sexual health) when dealing with menopause or sexual dysfunction?
 - a. Always
 - b. Often
 - c. Sometimes
 - d. Rarely
 - e. Never





Menopause: Extremely Brief Overview

What / When / Why

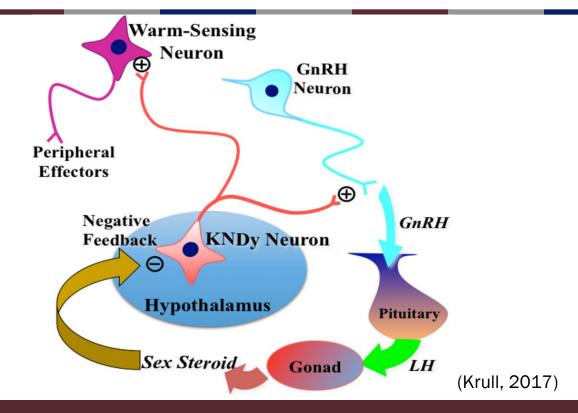


(Magalhaes & Atala, 2019)





Neuroendocrinology of Menopause







Stages of Menopause

Menarche FMP (0) Stage -5 -3b -3a -2 +1 a +1b +1c +2 -4 -1 Terminology REPRODUCTIVE MENOPAUSAL POSTMENOPAUSE TRANSITION Early Peak Late Early Late Early Late Perimenopause Duration variable variable 1-3 years 2 years 3-6 years Remaining (1+1)lifespan PRINCIPAL CRITERIA Menstrual Variable Regular Regular Subtle Variable Interval of to regular changes in Length amenorrhea Cycle Flow/ Persistent of >=60Length ≥7- day days difference in length of consecutive cycles SUPPORTIVE CRITERIA Endocrine 1 >25 IU/L** T Variable Variable* Variable* Stabilizes **FSH** Low Very Low Low Low Low Low Low AMH Very Low Low Low Low Low Inhibin B Antral Follide Very Low Very Low Low Low Low Low Count DESCRIPTIVE CHARACTERISTICS Symptoms Vasomotor Vasomotor Increasing symptoms symptoms symptoms of Likely Most Likely urogenital atrophy * Blood draw on cycle days 2-5 ↑ = elevated **Approximate expected level based on assays using current international pituitary standard⁶⁷⁻⁶⁹

(Norris et al, 2023)





How it started...

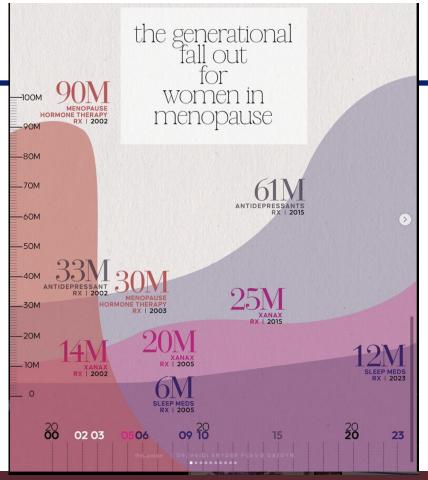
- In the 80's & 90's observational studies and meta-analyses showed menopausal hormone therapy (MHT) beneficial in preventing cardiovascular disease, osteoporosis, dementia and decreased allcause mortality
- 1992 American College of Physicians recommended MHT for prevention of coronary disease - "All women, regardless of race, should consider preventive hormone therapy"
- 1998 Heart and Estrogen/Progestin Replacement Study (HERS)
- 2002 Women's Health Initiative (WHI) Study

(Lobo et al, 2016)





How it started ... (continued)



(https://www.instagram.com/p/Corh0460 8sf/?img_index=3, n.d.)





What Happened?

WHI

- Randomized controlled clinical trials (RCT) primary prevention congenital heart disease (CHD), Non-fatal myocardial infarction (MI), CHD Death
- 27,347 women, aged 50-79, average age 63
- Intact uterus 16,608 women
 - √ 0.625mg Conjugated Equine Estrogen (CEE) + 2.5mg MedroxyProgesterone Acetate (MPA)
- Status post (s/p) Hysterectomy 10,739 women
 - **√** 0,625mg CEE
- 35% overweight, another 34% obese
- 35% hypertensive
- >45% past or current smokers

(Lobo et al, 2016)





Women's Health Initiative (1 of 3)

97.5%

of women in the EE + MPA arm had absolutely NO problems

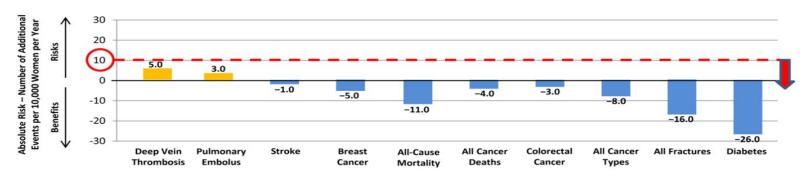
(Manson et al, 2024)



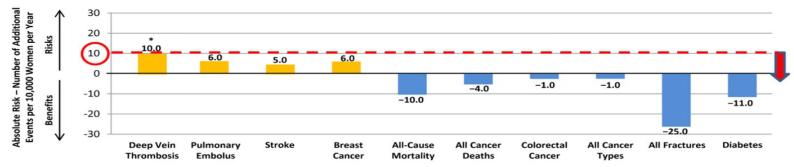


Women's Health Initiative (2 of 3)

CEE Alone Trial



CEE+MPA Trial



(Lobo et al, 2016)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9178928/





Women's Health Initiative (3 of 3)

Age

■ 50-59: 30% reduction in all cause mortality

■ 60-69: Null benefit

■ 70-79: Increased all-cause mortality

 And so was born, together with the Danish Osteoporosis Prevention Study (DOPS), Kronos Early Estrogen Prevention Study (KEEP) and Early versus Late Intervention Trial with Estradiol (ELITE) trials, the

Timing Hypothesis

Decreased CHD

Prevention of new onset diabetes mellitus (DM)

Decreased all cause mortality

Prevention of osteoporosis

(Manson et al, 2013; Bhupathiraju & Manson, 2014)





DOPS Trial

- Danish Osteoporosis Prevention Study 1990/1993 August 2002 (planned 2013)
- Ten year partly RCT, with six additional years follow up
- 1,006 perimenopausal or recently menopausal women, average age 50 (45-58)
 - Intact uterus Oral Estradiol 2mg + oral sequential Norethindrone acetate 1mg
 - o S/P hysterectomy Oral Estradiol 2mg
- Two key questions:
 - o Can hormone replacement therapy (HRT) prevent osteoporosis and related fractures in postmenopausal women?
 - Does HRT provide broader health benefits, such as reducing heart disease risk, and are there any long-term risks?
- After 10-year RCT: MI + heart failure (HF) reduced by 52%, Total Mortality reduced by 43%
- No differences in incident breast cancer, stroke or venous thromboembolism (VTE) between treatment groups

(Mosekilde et al, 1999)





KEEPS Trial

- Danish Osteoporosis Prevention Study 1990/1993 August 2002 (planned 2013)
- Kronos Early Estrogen Prevention Study 2005-2009 (planned 2010)
- Four year Randomized, double-blind, placebo-controlled trial
- To assess the effects of early initiation of hormone therapy on cardiovascular (CV) health, cognitive function, and quality of life in recently postmenopausal women.
- 727 healthy, recently menopausal (3 years) women. Average age 52 (42-58)
- Exclusion: Women with a history of cardiovascular disease, uncontrolled hypertension, or DM
 - Oral CEE 0.45 mg + 200mg cyclic micronized progesterone
 - Transdermal Estradiol 0.05mg + 200mg cyclic micronized progesterone
 - Placebo: Control group receiving no hormones.
- In WHI, CV risk increased for the first year and then decreased back to baseline.

(Harman et al, 2005)





KEEPS Trial

Cardiovascular Health:

- Progression of Atherosclerosis: Assessed by measuring carotid intima-media thickness (CIMT) and coronary artery calcium (CAC).
- No difference in progression of atherosclerosis between hormone therapy (HT) and placebo.
- HT was safe for cardiovascular outcomes.

Cognition:

- Assessed through neuropsychological tests to evaluate memory, executive function & overall cognition.
- No improvements or harms to memory or cognition across all groups.

Quality of Life:

- Measurements: Symptoms such as hot flashes, sleep quality, mood, and sexual function.
- HT reduced vasomotor symptoms (hot flashes) and improved sleep.
- Transdermal Estradiol had greater benefits for sexual function.

Safety:

- No increase in breast cancer.
- Slightly elevated clot risk with oral estrogen but not transdermal.

(Harman et al, 2005)





ELITE Trial

- Early versus Late Intervention Trial with Estradiol
- Randomized, double-blind, placebo-controlled trial. Median follow-up of five years.
- Assess if timing of MHT initiation affects progression of atherosclerosis, measured by right common carotid intima-media thickness (CIMT) measured q6 months
- Secondary outcome coronary artery atherosclerosis by cardiac computed tomography at study end
- 643 healthy postmenopausal women:
 - o Early Postmenopause: < 6 years since menopause.
 - Late Postmenopause: > 10 years since menopause.
 - 1 mg oral estradiol daily + 45 mg vaginal progesterone gel x 10 days/mth
 - Placebo pills + placebo vaginal gel.
- Primary Endpoint: Rate of progression of carotid intima-media thickness (CIMT), a marker of subclinical atherosclerosis.

(Hodis et al, 2015)





ELITE Trial (continued)

• Findings:

- o HT slowed atherosclerosis progression when started < 6 years post menopause
- No significant difference in CIMT progression when started >10 years
- o No significant differences in VTE or breast cancer were observed between the treatment and placebo groups during the trial.

• Clinical Implications:

- Timing Matters: Starting HT early slows atherosclerosis progression.
- No cardiovascular harm when started late, but no benefit either.
- o Supports the "Timing Hypothesis": A "window of opportunity" for HT's cardioprotective effects exists early after menopause.

Takeaway:

 Early HT may slow cardiovascular aging, while late HT has neutral effects. Timing is critical for maximizing HT benefits.

(Hodis et al, 2015)





The Timing Hypothesis

- Cardiovascular effects of MHT depend on when it is initiated The window of opportunity!
- Early Initiation (<10 Years):
 - May slow atherosclerosis progression and improve cardiovascular health.
 - Likely linked to healthier blood vessels and less vascular damage early in menopause.
- Late Initiation (10-20 Year):
 - HT shows neutral effects on cardiovascular outcomes.
 - Advanced vascular aging and subclinical disease may limit HT's effectiveness.
- Later Initiation (>20 years):
 - CEE +/- medroxyprogesterone acetate are pro-inflammatory towards the endothelium and arterial plaques

(Lobo et al, 2016)





What is Perimenopause?

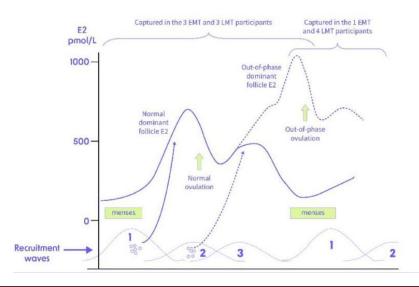
- Definition
 - The transitional phase leading to menopause, lasting 4-10 years before the final menstrual period.
 - Average age mid-40s
- Two Phases
 - Early Perimenopause: Persistent 7-day variation in menstrual cycle length.
 - Late Perimenopause: Prolonged intervals (≥60 days) between periods.





Physiology of Perimenopause

Physiology of the Menopause Transition



Early Menopause Transition

- Persistent cycle irregularity by ≥ to 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

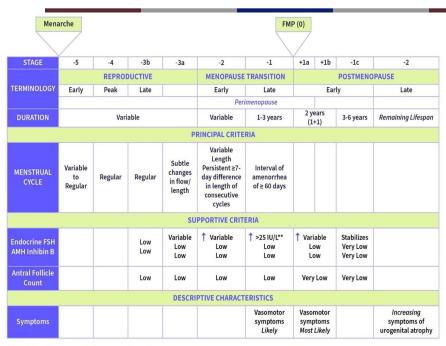
- Amenorrhea > 60 d.
- Menstrual cycles have variable cycle length
- Variable estradiol levels with increased prevalence of anovulation
- FSH levels are ≥ IU/L because of few remaining oocyes.
- Negligible AMH and AFC.
- LOOP cycles occur in a third of women; VMS and other signs of menopause likely

(The North American Menopause Society, 2024)





Straw-10



Criteria can not be applied

- History of premature ovarian failure
- Irregular menses
- Hysterectomy
- Endometrial ablation

STAGE	-2	-1
TERMINOLOGY	MENOPAUSE TRANSITION	
	Early	Late
	Perimenopause	
DURATION	Variable	1-3 years
	RINCIPAL CRITE	RIA
MENSTRUAL CYCLE	Variable Length Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of ≥ 60 days
	PPORTIVE CRIT	ERIA
Endocrine FSH AMH Inhibin B	Variable Low Low	↑ >25 IU/L** Low Low
Antral Follicle Count	Low	Low
	PTIVE CHARACT	ERISTICS
Symptoms		Vasomotor symptoms Likely

(The North American Menopause Society, 2024)





^{*} Blood draw on cycle days 2-5 = elevated

^{**} Approximate expected level based on assays using current international piluitary standard

Estrogen & Health: The Organs that Feel the Loss

The G protein-coupled oestrogen receptor (GPER) regulates many physiological functions (white background) and is involved in multiple pathologies and diseases (pink background) CKD, chronic kidney disease; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; PAH, pulmonary arterial hypertension; VSMC, vascular smooth muscle cell.

Central nervous system . Pain perception · Malignant melanoma . T cell development Thymus growth
 Thymic strophy Thyroid
• Folloular cell growth . Thyroid sancer Arterial system · Blood pressure Vascular tone . Arterial hypertension · Anti-inflammation * Atherosclerosis a Fatal immunity · Infection . Autoimmune diseases Coronary arteries . Coronary artery tone . VSMC growth . Coronary artery disease Bone trabecularization Myocardial infarction Osteochondritis Osteoporosia Cardiomyocyte growth Myocardial contractilis . Pulmonary VSMC growth · Reperfusion injury Myocardiai filorosia . Heart failure Mammary gland

• Epithelial cell proliferation · Hepatocyte proliferation · Breast cancer Lipid metabolism * NAFED * MASH Cartilage . Chandrocyte differentiation Gall bladder · Cholesterni crystalliza * Gall stones . Castric chief cell growth Epithelial metapliasi · Gastric cancer B-Cell survival Insulin secretion · Insulin resistance · Natriuresis · Renovascular function . Tubular cell proliferation Filomer (conterns)s Adipose tissue . Insulin function Lipid storage · insulin resistance e Obserty · Intestinal motility · Crohn's disease . Visceral hypersensitivity Ovaries • Ovalation . Overian cysts Skeletal muscle . Muscle strength . Exercise capacity · Myometrial contractility

(Prossnitz & Barton, 2023)





Key Points and Changes in Perimenopause

- Average onset: mid-40s, although age can vary.
- Some women can experience symptoms as early as the mid to late 30's.
- Menstrual irregularity is the hallmark sign.
- Many women first experience mood changes, vaginal dryness and sleep disruptions.

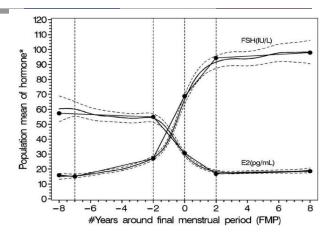




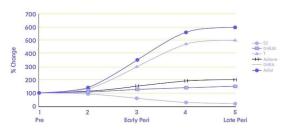


Hormonal Shifts in Perimenopause

- Hormones Involved
 - Fluctuations in estrogen and progesterone levels
 - ✓ Progesterone declines
 - √ Estrogen is volatile with highs and lows
 - Follicle-Stimulating Hormone (FSH) levels increase as ovarian reserve declines
 - Anti-müllerian hormone (AMH): Decreases, reflecting declining ovarian reserve
 - Testosterone levels decrease
 - Cortisol increases late perimenopause with FSH
- Key Effects
 - Irregular ovulation and menstrual changes
 - Mood changes, sleep disruption, GSM







(The North American Menopause Society, 2024)





Common Symptoms in Perimenopause

- Physical Symptoms:
 - Hot flashes, night sweats, sleep disturbances
 - Irregular periods and heavy bleeding
 - Vaginal dryness, pain with intimacy
- Emotional Symptoms:
 - Mood swings, irritability, depression
 - Worsening premenstrual syndrome
 - Anxiety
 - Low libido
- Cognitive Changes
 - Brain Fog
 - Memory issues





Diagnosis of Perimenopause

- Clinical Diagnosis:
 - Based on symptoms and menstrual changes
 - √ This can be challenging in the patient not having a menses (ie: hysterectomy, intrauterine device [IUD], ablation)
 - No single test confirms perimenopause
- Blood Tests (Optional):
 - Hormone levels: FSH, estradiol, AMH
 - Thyroid function to rule out other conditions





How to Treat Perimenopause

Hormonal Options

- Need contraception?
 - ✓ Oral contraceptive pill (OCP)
 - ✓ Progestin only Pill (POP)
 - ✓ Drospirenone/estetrol
 - ✓ IUD
 - √ Birth control vaginal ring
 - √ Subdermal implant
- Bleeding issues?
 - ✓ OCP
 - / POP
 - √ IUD
- Menopausal dosing HT?
 - √ Micronized progesterone
 - ✓ Estradiol
 - √ Estradiol + Micronized progesterone





How to Treat Perimenopause (continued)

Lifestyle Interventions:

- Regular exercise
 - ✓ Exercise helps manage weight, improve mood, reduce hot flashes, strengthen bones, and protect heart health
- Stress reduction
 - ✓ Managing stress through mindfulness, meditation, or yoga can lower cortisol levels, improve sleep, and reduce anxiety and mood swings
- Sleep hygiene
 - ✓ Prioritizing consistent sleep patterns, creating a cool and dark sleep environment, and limiting screen time can improve energy levels and reduce night sweats
- Avoiding triggers like caffeine and alcohol
 - √ Can minimize hot flashes, improve sleep quality, and stabilize mood and energy levels





Perimenopause Pearls

- Cycling Progesterone
 - Cycle for 12-14 days starting on day 1 or day 15 or can do continuous
- Cycling Estradiol
 - Cycling the week prior to menses when patients are most symptomatic.
- Vaginal estradiol
 - Can be used in perimenopause, or cycled week prior to menses
- What if in a LOOP cycle
 - This can lead to very high estradiol levels; patients can stop their estradiol for a period of time to see if they feel better
- Using continuous OCP, no need to have a monthly withdrawal





Common Perimenopause Myths

You can not treat with MHT

- Women do not have to wait until menopause to use menopausal hormone dosing
- You can not get pregnant in perimenopause
 - Women need adequate contraception, while the likelihood in late perimenopause is low, it is not zero

You're too young to have symptoms

■ While the average age may be in the 40's, it is not unusual to see these symptoms start in the mid to late 30's

You're still having periods so you are not there

 Perimenopausal women can have regular, heavy, light or skipped menses and can greatly benefit from treatment

You have to wait until menopause to be treated

 No need to wait, there is no data to support that women need to wait until menopause for treatment

Perimenopause is the same for all women

- This, like every aspect of treating midlife women, is very nuanced
- Each women is different and may respond different to treatments
- Treatment is often trial and error and open communication with patients to discuss this is very important





Perimenopause Health Implications

Bone Health:

- Decline in estrogen affects bone density
- Increased risk of osteoporosis
- Bone loss begins in perimenopause, with an average loss of 10-12% at hip and spine across menopause transition equal to 1 T score
- After transition the rate decreases to 0.5% per year
- Age 50 women have lost 15.5% of bone mass
- Age 80 women have lost 30% of bone mass

Cardiovascular Health:

 Higher likelihood of cardiovascular changes (e.g., cholesterol and blood pressure fluctuations)

Urogenital:

 Potential for urogenital symptoms like urinary incontinence, urgency and vaginal dryness



(https://github.com/quantori/edema-quantification, n.d.)





1.8% of Women Take MHT Today

Issue	Call to action
Society is bombarded with information on menopause that is often inconsistent, inaccurate, and/or harmful.	All parties must attempt to present a clear, consistent, and evidence-based message about the safety of FDA approved HT options.
Most providers have inadequate training, or retraining, in caring for women experiencing menopausal symptoms.	Physicians need education, experience and exposure through focused medical school and residency training programs.
Menopause is socially charged, affecting the way menopause is experienced in the home, the workplace, the media, and at the doctor's office	Health care professionals can partner with women to demand an improvement in care from their support networks, employers, the media, and the medical professions' attitude surrounding midlife women's health

(Hirsch, 2021)





Menopausal Hormone Therapy...Where Do I Start?

- Does she need contraception? (IUD/POP/combined oral contraceptive)
- Any labs helpful?
- Preventative care up to date?
- Reproductive history, any history trauma, postpartum depression (PPD) or premenstrual dysphoric disorder (PMDD)? Hypothyroid?
- Menopause Questionnaire
- GSM on it's own or any systemic symptoms?
- Any red flags?
- What has she tried before? Over-the-counter medications? Supplements? Compounded?
 Pellets?
- Does she have a uterus, a progestin IUD or endometriosis? (needs oral progesterone?)
- Still having periods? (Sequential vs. Continuous MHT)

(Pinkerton et al, 2014)





Labs and Rads

Hormonal Labs

- Estradiol, total testosterone, sex hormone binding globulin (SHBG), full thyroid panel
 - ✓ Perimenopause: FSH, AMH

Metabolic Labs

- All: lipids, comprehensive metabolic panel (CMP), complete blood count (CBC), HgbA1c, C-reactive protein (CRP)-HS
- Over 60 years old/>10 years PM: Lp (a), Apolipoprotein B-100 (APO-B)

Nutrients

■ Ferritin, Vit D, B12, folic acid

Radiology

- Mammogram (MMG), dual x-ray absorptiometry (DEXA) at menopause transition
- If > 60 years old/>10 years PM: CAC





Labs and Rads (continued)

Hormonal Labs

- Estradiol, total testosterone, SHBG, full thyroid panel
 - ✓ Perimenopause: FSH, AMH

Metabolic Labs

- All: lipids, CMP, CBC, HgbA1c, CRP-HS
- Over 60 years old/>10 years PM: Lp (a), APO-B

Nutrients

Ferritin, Vit D, B12, folic acid

Radiology

- MMG, DEXA (at menopause transition)
- If > 60 years old/>10 years PM: CAC





FDA approved indications for MHT

- Treatment of Vasomotor Symptoms
- Prevention of Osteoporosis
- Treatment of Premature Ovarian Insufficiency
- Genitourinary Syndrome of Menopause

Most women are a candidate for MHT and have at least one of these issues!





Prescribing Stoplight Chart



(https://www.colourbox.com/vector/pedestrian-traffic-light-cartoon-vector-64618735, n.d.)

Safety Considerations for Prescribing HT

Red Lights	Yellow Lights (think transdermal)	Green Lights
High Risk	Intermediate Risk HT	Low Risk HT
Estrogen Receptor + Breast Cancer	Hypertension	Low risk for breast cancer
Active liver disease- cirrhosis	Uncontrolled Dyslipidemia	Final menstrual period within 10 years
Spoke, TIA or MI	Diabetes Hgb A1C > 8	Normal Weight
Life threatening blood clot: DVT or PE	TIA without residual effects	Normal blood pressure
Prior hormone induced clots (pregnancy induced DVT, clot on HT)	Smoking	Physically active
High-risk endometrial or ovarian cancer	History of DVT from trauma	10-yr ASCVD risk <5%
Congenital heart disease	Thyroid medications (monitor levels)	
10-yr ASCVD risk ≥ 10%	Previous HT use but off now for > 10 years	
ASCVD/CAD/PAD	Migraines	
	Auto-immune conditions	
	High-risk genetic mutations for cancer	
	Non-gynecologic cancers	
	Factor V Leiden (heterozygous vs. homezygous)	
	Obesity	
	10 year ASVD risk > 5-10%	





		anouchina Londaloi							
Estradiol Patches*									
17beta (17β)-estradiol Vivelle- Dot/Dotti/Lyllana/Minivelle	0.014mg* Menostar	0.025mg/day	0.0375-0.5mg /day	0.075-0.1mg/day					
Combined Patches*							–		
17β (E) + LNG (P): change once weekly Climara			0.45mg/0.015mg		l Optio	ns: Pi	IIS. Pa	atches	S.
17β (E) + NETA (P: change twice weekly Combipatch		0.05mg/0.14mg	0.05mg/0.25mg						-,
Gel- daily dose					Chron	ys, Ge	lo or	Dingo	
17β (E)Gel Divigel	0.25g	0.5g	1g	1.25g	ı Surav	VS. GE	15 OF	RIIIES	
17β (E)0.06% (0.52mg/pump) Elestrin	1 pump		2 pumps			, , ,		80	
17β (E)0.06% gel (0.75mg/ pump) EstroGel		1pump	2 pumps]				
Spray									
17β (E)(1.53mg/actuation) Evamist		1 spray	2-3 sprays		1				
v	aginal Ring (only vagir	nal product with syste	mic effects)				0.3 or 0.45 mg E +	0.625mg E + 2.5 P or	
17β (E) Vaginal Ring Femring			0.05mg	0.1mg	CE (E)+MPA (P) Prempro		1.5mg P	5.0 P	
	Oral	Pills-daily use			EE (E) +NETA (P) Fyavolv/Jinteli			2.5 μg E + 0.5mg P	5 μg E + 1mg P
					17β (E) + drospirenone (P)				
17beta (17β)-estradiol					Angeliq		0.5mg E + 0.25 P	1mg E + 0.5mg P	
17β (E) Estrace		0.5mg	1mg	1.5-2mg	EE (E) + methyltestosterone				1.25mg/2.5mg
Conjuagated estrogens (CE) Premarin		0.3mg	0.45-0.625mg	0.9 - 1.25mg	Intermittent-Combined Regime				
Esterified estrogens (EE) Menest Combined Oral Pills		0.3mg	0.625mg	0.9-1.25mg	17β (E) + norgestimate (P)			1mg E + 0.09mg P	E alone for 3d, followed by E+P for 3d, repeated continuously)
Continuous-Cyclic Regime									
CE (E) + MPA (P)			0.625mg E + 5.0 mg (P)	(E only days 1-14, E+P days 15-28)	Abbreviations:				
Continuous Combined Regime			, ,	,,	17β (17beta-estradiol, CE (E) (conju		gen), LNG (levonorge	strel), MPA (medroxypr	ogesterone acetate),
17β (E) + NETA (P) Activella/					NETA (norethindrone acetate), P (Pr	0 ,			
Amabelz/Mimvey**		0.5mg E + 0.1mg P	1mg E + 0.5 mg P**		*Patches: Estradiol 0.014mg and Es		ge once weekly: all oti	ners change twice week	dy
					*only for prevention of osteoporosis				
17β (E) + Progesterone (P) Bijuva			1mg E + 100mg P		^In special circumstances, women w	ith decreased libido ma	y benetit from the add	lition of combined estro	gen/testosterone

Standard Dose

(Moderate)

Low

Topical/Transdermal Estradiol

High

Very Low





Progestogen Dosing

	Minimur	n Progestogen Dosing]			
Daily Oral Dosing						
Medroxyprogesterone acetate	0.5-1mg/2.5mg	0.5-1mg/2.5mg	0.5-1mg/2.5mg	1mg/ <mark>5</mark> mg		
Norethindrone	0.35mg	0.35mg	0.35mg	0.7mg		
Norethindrone acetate	2.5mg	2.5mg	5mg	5mg		
Micronized Progesterone	100mg	100mg	100mg	200mg		
Slynd	4mg	4mg	4mg	4mg		
Cyclic Oral Dosing (12-14 days	/mo) or Pulsed 3 days	s on and 3 days off				
Medroxyprogesterone acetate	5mg	5mg	5mg	5mg		
Norethindrone	0.35-0.7mg	0.35-0.7mg	0.35-0.7mg	0.7mg		
Norethindrone Acetate	2.5mg	2.5mg	2.5mg	5mg		
Micronized Progesterone	200mg	200mg	200mg	200mg		
Intrauterine						
Levonorgestrel	6-20µg/d	6-20μg/d	6-20µg/d	6-20μg/d		
Vaginal						
Crinone 4%/8%	45mg	45mg	45mg	90mg		

Abbreviations:

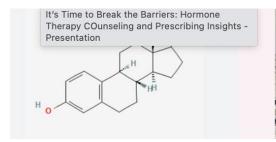
17β (17beta-estradiol, CE (E) (conjugated equine), E (Estrogen), LNG (levonorgestrel), MPA (medroxyprogesterone acetate), NETA (norethindrone acetate), P (Progesterone)

*Patches: Menostar and Climara pro: change once weekly; all others change twice weekly





MHT Side Effects







Estrogen

- Bloating
- Bad mood
- Bleeding
- Breast tenderness

Progesterone

- Bloating
- Sluggishness
- Fluid Retention
- Sleepiness

Testosterone

- Ache
- Oily Skin
- Facial Hair
- Coarse Skin at application site

(https://pubchem.ncbi.nlm.nih.gov/compound/667515, n.d.; Photo courtesy of Dr. Kress, n.d.; https://ssl.adam.com/content.aspx?productid=, n.d.)





Selective estrogen receptor modulators (SERM): Bazedoxifene/CEE: Duavee

- Estrogen receptor agonist-antagonists (ERAA)
- 20mg Bazedoxifene (BZD) with 0.45 CEE
- SMART Trials:
 - Effective and safe treatment for menopausal symptoms in women with intact uterus
 - FDA approved to treat VMS and prevent osteoporosis
 - Use with patient's s/p bilateral salpingo oophorectomy (BSO) for BRCA or LYNCH
 - BXD competitively inhibits binding of 17-B estradiol-antagonist at uterus
 - Carries similar risk of deep vein thrombosis (DVT) as MHT
 - Use with patient's s/p BSO for BRCA or LYNCH

(Pinkerton et al, 2014)





Testosterone Therapy

- Endorsed for Hypoactive Sexual Desire Disorder
- No product FDA approved for women
- Androgens are responsible for the functioning of cardiovascular, muscular, skeletal and reproductive systems.
- Safety data show no serious adverse events with physiologic testosterone use, but long-term safety has not been established.
- Global Position Statement: clinical guidance regarding the use of testosterone therapy in women, examining the effect on sexual function; well-being, mood, and cognition; musculoskeletal effects; cardiovascular and breast health
- Check total testosterone, CMP and lipids every 3 months x 1 year then annually if stable

Rx: Testosterone gel 50gm/5ml 1% rub 5gm to inner thigh every morning or evening #30 tubes/0RF.

- Instruct transfer to 5ml syringe & dose
 0.5ml/night
- o A tube should last 10-12 days

(Davis et al, 2019)





Prescribing Pearls

- Low and slow
- Typically start with whatever hormone will treat the majority of symptoms
 - Typically start with progesterone
 - Perimenopausal women do not need progestogen
 - Women without a uterus can have progesterone for mood and sleep benefits
- Allergy to peanuts-need compounded progesterone
- Labs are handy if symptoms are not improving to check for absorption





Timing & Duration of Use

- The American College of Obstetricians and Gynecologists and The Menopause Society have expanded their treatment definition to state that women on HT do not need to stop treatment at age 65.
- Often, symptoms return.
- Consider lower doses with aging due to decreased metabolism





Non-Hormonal Options for VMS

FDA Approved:

- Brisdelle 7.5 mg at night (Paroxetine) or Paroxetine 10 mg
- 7.5 mg low dose not associated with weight gain or sexual dysfunction
- SSRI's (paroxetine, fluoxetine, C/I with use of tamoxifen (renders less effective)

Several off-label options for VMS:

- Citalopram 10-20 mg lowest effective dose
- Escitalopram 5-20 mg lowest effective dose
- Desvenlafaxine: 50 100 mg lowest effective dose
- Venlafaxine 37.5-75 mg: lowest effective dose
- Gabapentin: 100 300 mg lowest effective dose
- Oxybutynin 5 mg BID: lowest effective dose
- Clonidine: 0.1 mg BID

Medication	Efficacy in Reducing HF Frequency vs. placebo			
Paroxetine salt (7.5 – 25 mg)	40 – 50 %			
Escitalopram 10 – 20 mg	30 – 45%			
Citalopram 10 – 20 mg	45-47%			
Venlafaxine 75- 100 mg	25-55%			
Desvenlafaxine 100- 150 mg	60 – 70%			
Gabapentin 900-2400 mg	40 – 45%			
Oxybutynin	25%			
Clonidine	20-35%			

(Hirsch & Manson, 2022; The Menopause Society, 2022; The Menopause Society, 2022; The North American Menopause Society, 2023)

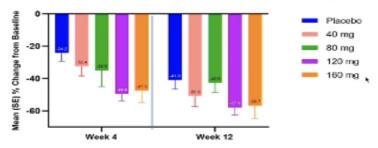




Fezolinetant

- Hypothalamic KNDy (Kisspeptin, Neurokinin B, & Dynorphin) neuron receptor antagonists.
 - Group of KNDy neurons modulate core body temperature. They hypertrophy in PM women, indicating a role in HF pathogenesis
 - SWITCH-1: RCT double-blind, placebo controlled 12-week trial of four doses of NT-814 once daily vs, placebo for VMS treatment
 - Well-tolerated, good safety profile

Significant improvements vs placebo in hot flash frequency with the 120 mg and 160 mg NT-814 once daily doses



(Trower et al, 2020)





Definition and Prevalence of Genitourinary Syndrome of Menopause (GSM)

- Definition
 - GSM encompasses the changes in the female genitourinary tract associated with menopause, including vaginal dryness, pain with intercourse, and urinary symptoms.

- Prevalence
 - Studies suggest that up to 75% of postmenopausal women experience up to one symptoms.

(Phillips & Bachmann 2021).





Anatomy and Physiology of Genitourinary Syndrome of Menopause (1 of 3)

- Vagina
- Vulva

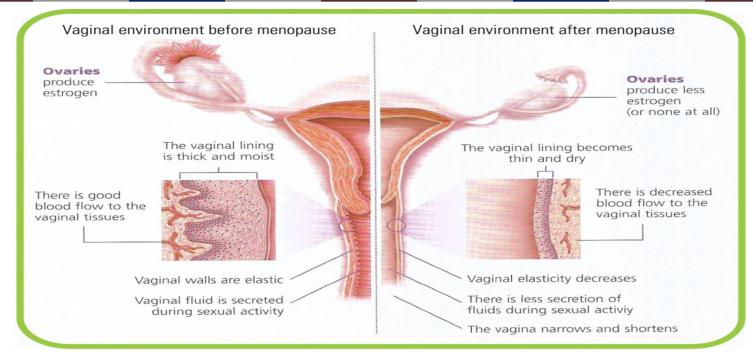
Urethra

Bladder





Anatomy and Physiology of Genitourinary Syndrome of Menopause (2 of 3)

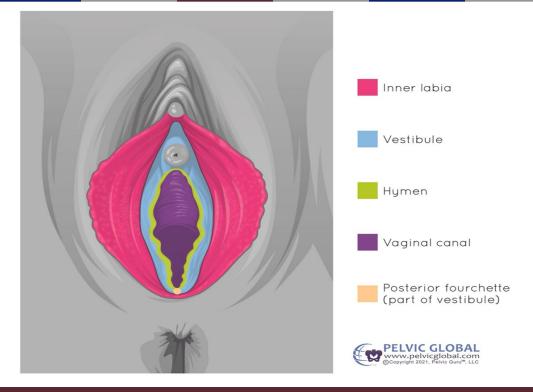


(Johnston, 2002)





Anatomy and Physiology of Genitourinary Syndrome of Menopause (3 of 3)

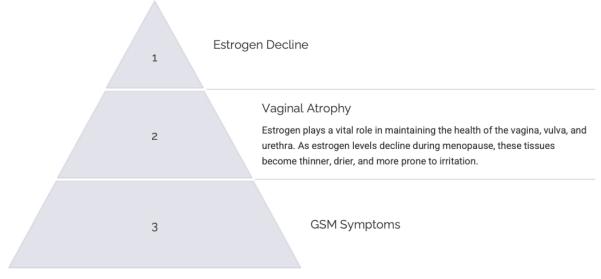






Hormonal Changes During Menopause

Hormonal Changes During Menopause



The North American Menopause Society. (2020). The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. *Menopause*, 27(9), 976–992. https://doi.org/10.1097/GME.00000000001609





Genitourinary Syndrome of Low Hormone State

Conditions resulting in a low estrogen state:

- Lactation
- Amenorrhea
- Oral Contraceptive Pill
- Premature Ovarian Insufficiency (POI)
- Ovarian surgery or a hysterectomy
- Chemotherapy
- Pelvic radiation
- Treatment with Aromatase Inhibitors or SERMS, eg. Tamoxifen





Impact of GSM on Sexual Function and Quality of Life

- Sexual Function
- Quality of Life

(Faubion et al. 2018)





Barriers to Assessing Care in the Military

- Limited access to Specialists
- Stigma and Shame

(McDermott et al. 2024)





Screening and Assessment of GSM in the Military Population

1. Medical History

Take a through medical history, including symptoms, past treatments, and sexual history

2. Physical Exam

Perform a physical exam, including a pelvic exam, to assess the vulva, vagina, and cervix

3. Patient Education

Educate the patient about GSM, its causes, symptoms, and treatment options





Treatment Options for GSM

- Hormonal
- Non-Hormonal
- Alternatives





Estrogen Therapy for GSM

- Vaginal Estrogen
- Topical Estrogen
- Oral Estrogen





Local Treatment of GSM

Mode Cream Brand names Premarin		Cream	Ring	Insert/Tablet	Insert	
		Estrace	E-string	Imvexxy, Yuvafem, Vagifem		
Dose	0.625mg conjugated estrogens	0.01mg estradiol	0.075mg/day estradiol	0.01mg estradiol	6.5mg/day DHEA	
Directions	1 gm every night for 2 weeks, then 1 gm twice a week	1 gm every night for 2 weeks, then 1 gm twice a week	Replace ring every 3 months	1 insert every night for 2 weeks, then 1 insert twice a week	1 insert every night	
Pros/Cons Some find it messy		Some find it messy Can be moisturizing	"Set it and forget it"	Yuvafem and Vagifem come with individual applicators	Some find it messy Can be moisturizing Helps the vestibule	





Local Treatment of GSM (continued)



(https://oafp.org/wp-content/uploads/OAFP-Lunch-Learn-GSM-Handouts.pdf, n.d.)





NAMS Position Statement

The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society

Abstract

Objective: To update and expand the 2013 position statement of The North American Menopause Society (NAMS) on the management of the genitourinary syndrome of menopause (GSM), of which symptomatic vulvovaginal atrophy (VVA) is a component.

Methods: A Panel of acknowledged experts in the field of genitourinary health reviewed the literature to evaluate new evidence on vaginal hormone therapies as well as on other management options available or in development for GSM. A search of PubMed was conducted identifying medical literature on VVA and GSM published since the 2013 position statement on the role of pharmacologic and nonpharmacologic treatments for VVA in postmenopausal women. The Panel revised and added recommendations on the basis of current evidence. The Panel's conclusions and recommendations were reviewed and approved by the NAMS Board of Trustees.

Results: Genitourinary syndrome of menopause affects approximately 27% to 84% of postmenopausal women and can significantly impair health, sexual function, and quality of life. Genitourinary syndrome of menopause is likely underdiagnosed and undertreated. In most cases, symptoms can be effectively managed. A number of overthe-counter and government-approved prescription therapies available in the United States and Canada demonstrate effectiveness, depending on the severity of symptoms. These include vaginal lubricants and moisturizers, vaginal estrogens and dehydroepiandrosterone (DHEA), systemic hormone therapy, and the estrogen agonist/antagonist ospemifene. Long-term studies on the endometrial safety of vaginal estrogen, vaginal DHEA, and ospemifene are lacking. There are insufficient placebo-controlled trials of energy-based therapies, including laser, to draw conclusions on efficacy and safety or to make treatment recommendations.

Conclusions: Clinicians can resolve many distressing genitourinary symptoms and improve sexual health and the quality of life of postmenopausal women by educating women about, diagnosing, and appropriately managing GSM. Choice of therapy depends on the severity of symptoms, the effectiveness and safety of treatments for the individual patient, and patient preference. Nonhormone therapies available without a prescription provide sufficient relief for most women with mild symptoms. Low-dose vaginal estrogens, vaginal DHEA, systemic estrogen therapy, and ospemifene are effective treatments for moderate to severe GSM. When low-dose vaginal estrogen or DHEA or ospemifene is administered, a progestogen is not indicated; however, endometrial safety has not been studied in clinical trials beyond 1 year. There are insufficient data at present to confirm the safety of vaginal estrogen or DHEA or ospemifene in women with breast cancer; management of GSM should consider the woman's needs and the recommendations of her oncologist.

https://menopause.org/professional-resources/position-statements

NAMS Position Statement (2020)





R	PRESCRIPTION
	Patient Name: Address:

Premarin 0.625mg Vaginal Cream

1gm vaginally nightly for 2 weeks,

then decrease to 1gm twice a week

Dispense: 42.5gm (1 tube)

Days supply: 90

Refills: Forever

Date:_____ Signature:





D , PRESCRIPTION
Patient Name: Address:
Estradiol 0.01% Vaginal Cream
1gm vaginally nightly for 2 weeks,
then decrease to 1gm twice a week
Dispense: 42.5gm (1 tube)
Days supply: 90
Refills: Forever
Date: Signature:









D , PRESCRIPTION
Patient Name:
Address:
Estradiol 10mcg Insert
1 insert vaginally nightly for 2 weeks,
then 1 insert twice a week
Dispense: First fill - 24 inserts
Subsequent refills - 24 inserts
Days supply: 90 Refills: Forever
Date: Signature:





D , PRESCRIPTION	
Patient Name:	
Address:	
Estradiol 4mcg or 10mcg soft gel Insert	
1 insert vaginally nightly for 2 weeks,	
then 1 insert twice a week	
Dispense: First fill - 18 inserts	
Subsequent refills - 24 inserts	
Days supply: 90 Refills: Forever	
Date: Signature:	
Date: Signature:	





PRESCRIPTION Patient Name: Address:
Prasterone (DHEA) 6.5mg
1 insert every night
Dispense: 84
Days supply: 84
Refills: Forever
Date: Signature:





D , PRESCRIPTION
Patient Name:
Address:
Estradiol 2mg Ring Insert 1 ring vaginally.
Replace every 90 days.
Dispense: 1 Ring
Days supply: 90
Refills: Forever
Date: Signature:





R PRESCRIPTION Patient Name:
Address:
Ospemifene 60mg
Take one tablet by mouth daily
Dispense: 90
Days supply: 90
Refills: Forever
Date: Signature:





D , PRESCRIPTION
Patient Name: Address:
Address
Estradiol 0.01% with Testosterone 0.1% in Versabase cream
Apply 0.25gm to the vulvar vestibule once a day every day
Dispense: 7.5gm - 1 month
15gm - 2 months
22.5gm - 3 months
Days supply: 90 Refill: None
Date: Signature:





FDA and Box Warning

Box Warning for increased risk of:

- Endometrial Cancer
- Invasive Breast Cancer
- Stroke
- DVT
- Pulmonary Embolism
- Myocardial Infarction
- Probable Dementia





Non hormonal Therapy GSM

- Lubricants
- Moisturizers
- Dilators





Key Takeaways (1 of 2)

- The perception and recommendations for menopausal hormone therapy (MHT) have evolved significantly since the publication of the Women's Health Initiative. The American College of Obstetricians and Gynecologists and The Menopause Society no longer mandate stopping hormone therapy at age 65, focusing instead on individualized, lifelong care.
- The "Timing Hypothesis" emphasizes the importance of starting MHT early (<10 years postmenopause) to maximize cardiovascular benefits and slow atherosclerosis progression. Late initiation provides neutral effects but does not exacerbate risks significantly.
- Effective treatment involves understanding individual patient needs, such as tailoring hormone therapy dosages and addressing specific symptoms like vasomotor instability or genitourinary syndrome of menopause (GSM). Lifestyle modifications and non-hormonal treatments complement hormonal therapies.





Key Takeaways (2 of 2)

- Significant barriers to effective menopause management include limited provider training and misconceptions about hormone therapy. Improved education and evidence-based resources are critical to overcoming these challenges and enhancing care quality.
- Modern formulations of hormone therapy, including low-dose and transdermal options, have demonstrated a favorable safety profile for appropriate candidates. Risks such as VTE are significantly lower with transdermal delivery systems compared to oral estrogens.
- Women may present with a wide range of menopausal symptoms, including vasomotor symptoms (hot flashes, night sweats), genitourinary syndrome of menopause (vaginal dryness, dyspareunia), sleep disturbances, mood changes, and cognitive complaints. These symptoms are often multifaceted and may overlap with other conditions, underscoring the need for comprehensive assessments to differentiate menopause-related changes from other potential causes. However, if a woman is between the ages of 30-65, perimenopause and menopause should be on the top of your differentials.





- 7. How confident are you in managing perimenopause-related symptoms (e.g., vasomotor symptoms, sleep disturbances) in female DoD patients?
 - a. Very confident
 - b. Somewhat confident
 - c. Neutral
 - d. Somewhat unconfident
 - e. Very unconfident





- 8. Do you now feel that the formal training has adequately prepared you to address menopause and sexual health in female patients?
 - a. Yes
 - b. No





- 9. What do you believe are the most significant barriers to managing perimenopause and menopause in military health care settings? (Select all that apply)
 - a. Time constraints
 - b. Stigma associated with sexual health concerns
 - c. Lack of specialized resources
 - d. Limited training on the subject
 - e. Cultural or institutional challenges





- 10. Do you now feel more equipped to discuss hormonal therapies (e.g., hormone replacement therapy) with female DoD patients experiencing menopause?
 - a. Yes
 - b. No
 - c. Uncertain





- 11. Do you feel that there is a stigma surrounding the discussion of sexual health and menopause in military health care?
 - a. Yes, significantly decreased
 - b. Yes, somewhat decreased
 - c. Neutral
 - d. No change
 - e. Stigma has increased





- 12. How often do you now plan to refer female patients for specialist care (e.g., gynecology, sexual health) when dealing with menopause or sexual dysfunction?
 - a. Always
 - b. Often
 - c. Sometimes
 - d. Rarely
 - e. Never





Questions?





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