Myths & Misconceptions:

Menopause, Perimenopause, and MHT

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Disclosures

1. **Co-Owner;** Director of Research and Education for Vitanica
2. **Scientific Advisory Boards:** Integrative Therapeutics, Symphony, Nutritional Fundamentals for Health
3. **Speaker's Bureaus:** Precision Analytical, Doctor's Data, Enzyme Science, Natural Factors

Medical Myths

To get us going!

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Don’t Swim After Eating

“Wait an hour after eating before you go swimming to prevent cramping”

- False. A normal-sized meal consumed before swimming will not cause cramping.
- It is possible to feel tired and fatigued after overeating, so maybe avoid swimming right after.

“Shaved hair grows back thicker and darker”

- False. Although your mom may have told you this as a young girl so you wouldn’t be so eager to start shaving your legs, it’s not true. Because the hair is newer, it may have not yet been bleached by the sun, and so it appears darker and thicker.

“If you go outside with wet hair on a cold day, you’ll catch a cold”

- False. Colds are caused by viruses, which you can’t get just from being outside in the cold. You may feel sick if you’re outside all day in the cold or rain — runny nose, chills, fatigue — but it’s not because of a virus. It’s because you can experience the same symptoms when you are chilled as when you are sick.

“Cracking your knuckles causes arthritis”

- False. A 30-year study showed this is not the case. However, knuckle cracking can lessen one’s grip strength because of repeated overstretching of the tendons.

Eight Glasses of Water/day

“You need to drink eight glasses of water every day, in order to stay hydrated”

- False. Being dehydrated isn’t great for your health, but the idea that we need to drink eight glasses (around two liters) of water in order to stay hydrated has no real scientific backing. Research suggests that health can be maintained with a much lower water intake.

MHT Myths

- Estrogen causes breast cancer
- Estrogen + progestogens significantly increase risk of breast cancer
- Screening mammograms must be done prior to MHT Rx
- Women who take MHT should stop by the age of 60
- Postmenopausal women can safely start taking MHT at any age
- Progesterone cream is an adequate delivery method to provide endometrial protection in women who take systemic estrogen.

Landmark and Important MHT Research to be Familiar with:

- HERS
- Nurses Health Study
- PEPI trial
- EPAT
- ERA
- WELL-HART
- WHI-EPT
- WHI-Estrogen only
- WHI f/u studies
- WHIMS
- Other estrogen only studies
- Million Women Study
- MIRAGE
- California Teacher's Study
- KEEPS
- KEEPS –Cog
- KEEPS- sleep
- Cache County
- Timing Hypothesis studies
- Health outcomes after d/c HRT
- MHT/VET-Danish Cohort
- VET safety

Landmark and Important MHT Research to be Familiar with:

- HRT-GYN cancers
- HRT-ovarian cancer
- French studies- OMP vs MPA
- HRT-young onset breast cancer
- HRT-breast cancer incidence
- ELITE trial
- ESTHER study
- HRT-CVD
- ERT-CVD
- WISDOM
- Danish CVD study
- Menopause HRT-Cochrane Review
- REPLENISH
- REJOICE
- SWAN
- WHI-OS
- MS-FLASH
- SMART
- Finnish HRT-AD
- JAMA 2020; 20 year f/u WHI
- Lancet HT Meta-analysis 2019

Position Statements and Consensus Recommendations

Position Statements

- NAMS HRT-menopause 2022; Menopause J
- NAMS Nonhormone therapy -2023; Menopause J
- NAMS – GSM- 2020; Menopause J
- NAMS-Osteoporosis 2021; Menopause J
- USPSTF HRT 2017

Consensus Guidelines

- Global Consensus- Testosterone 2019; Climacteric
- Evaluation and Treatment of Perimenopausal depression 2018; Menopause J
- Management of GSM in women with or at high risk for breast cancer 2018
- Menopausal HT, Endocrine Society 2015
- Global Consensus Statement Menopausal HT-Climacteric 2016 (International Menopause Society)

Definitions: Perimenopause/Menopause

“You have to have VMS to be diagnosed as perimenopausal”

- False.

Perimenopause

ill-defined time period that surrounds the final years of a woman's reproductive life. It begins with the first onset of menstrual irregularity and ends after 1 year of amenorrhea has occurred, thereby defining the final menstrual period (FMP). There are two stages to the perimenopause or menopausal transition: the early transition, where cycles are mostly regular, with relatively few interruptions, and the late transition, where amenorrhea becomes more prolonged and lasts for at least 60 days, up to the FMP.

Menopause

No menses for 12 consecutive months; FSH > 25

STRAW+10

	Menarche						FMP (0)			
Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+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				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	↑ Variable* Low Low	↑ >25 IU/L** Low Low	↑ Variable Low Low		Stabilizes Very Low Very Low	
Antral Follicle Count			Low	Low	Low	**Low**	Very Low		Very Low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms *Likely*	Vasomotor symptoms *Most Likely*			*Increasing* symptoms of urogenital atrophy

* Blood draw on cycle days 2-5 ↑ = elevated

**Approximate expected level based on assays using current international pituitary standard[67-69]

Harlow SD, et al. Menopause. 2012;19(4):387-395.

Perimenopause/Menopause

Signs & Symptoms

Perimenopause/Menopause: Signs & Symptoms

Classic symptoms

- Change in menstrual cycle pattern (during perimenopause)
- Vasomotor symptoms (VMS; hot flashes and night sweats)
- Vulvovaginal symptoms, dyspareunia
- Sleep disturbances
- Psychological symptoms (depression, anxiety, moodiness)
- **There is no one universal menopause syndrome**

Avis NE, et al. Am J Med. 2005;118(suppl 12B):37-46; National Institutes of Health. Ann Intern Med. 2005;142:1003-1013; Bromberger JT, et al. Psychol Med. 2011;41(9):1879-1888; Cohen LS, et al. Arch Gen Psychiatry. 2006;63(4):385-390; Freeman EW, et al. Arch Gen Psychiatry. 2004;611(1):62-70.

Perimenopause/Menopause: Signs & Symptoms

Symptoms Elsewhere

- S. Africa: mood disorders, sexual dysfunction, osteo-muscular pain
- US: VMS, joint and muscle pains
- Australia: VMS, genitourinary dysfunction
- Asia: Depressive disorders
- Europe: sleep and depressive disorders

Perimenopause/Menopause: Signs & Symptoms

Other changes

- Changes in weight distribution; weight gain abdomen
- Cognitive changes brain fog, (memory, concentration, brain fog)
- Skin changes: collagen declines, dry, wrinkles, acne
- Dental changes: tooth loss, gum loss, dry mouth, burning mouth
- Ocular changes: dry, vision changes, blurred vision, edema, redness, cataracts
- Hearing changes: decline
- Hair changes: rogue hairs, hair thinning
- Fatigue
- Sexual dysfunction
- Swelling of hands or feet
- Bloating
- Aching joints
- Palpitations
- Brain fog

Breast Cancer & MHT

Breast Cancer & MHT

“Estrogen causes breast cancer”

“Estrogen + Progestins significantly increase risk of breast cancer”

- Myth.

Breast Cancer & MHT

- Breast cancer: one in eight US women
- Need an understanding of the potential effect of HT on breast cancer risk.
- Understand differences: ET, EPT, OMP vs MPA on breast tissues
- Different types of estrogen or progestogen
- Different formulations
- Timing of initiation
- Duration
- Progestogen use
- Select patient characteristics may play in breast cancer risk and MHT

Breast Cancer & MHT

Estrogen-Progestogen

- WHI: daily continuous combined CEE/MPA = increased risk of breast cancer (rare absolute risk), with 9 additional breast cancer cases per 10,000 person years of therapy. Found after 5.6 years- considered significant in nominal statistical terms; non significant when adjustments were made for multiple risk factors. (JAMA 2013;310)
- This 1.29 of the CEE + MPA in the WHI is considered not statistically significant
- Slight Increase appears to begin at 3-4 years, and remains elevated at 20 years cumulative f/u post intervention. (JAMA 2020;324)
- Post analysis: increased incidence of breast cancer was limited to women who had prior exposure to HT; in women without prior exposure to HT- breast cancer incidence was not significantly affected by CEE/MPA over 11 years of r/u including a mean intervention time of 5.6 years.
- **Risk in WHI is less than 1 additional case of breast cancer per 1,000 users, annually… A risk slightly greater than that observed with one daily glass of wine, less than two daily glasses, and similar to the risk reported with obesity and low exercise.**

WHI Review`E + P: RISK vs Benefits

	HRT	Placebo	Difference
Breast Cancer	3.8	3.0	+26%
Heart Diagnosis	3.7	3.0	+23%
Stroke	2.9	2.1	+38%
Clots	2.6	1.3	+100%
Hip Fracture	1.0	1.5	- 33%
Colon Cancer	1.0	1.6	-37%

JAMA 2002;288:321-333

WHI Estrogen Only: Hazard Ratios

	Ratio
Coronary Heart Disease	0.91
Stroke	1.39
Pulmonary Embolism	1.34
Deep Vein Thrombosis	1.47
Breast Cancer	0.77
Colorectal Cancer	1.08
Hip Fracture	0.61
Vertebral Fracture	0.62
Total Fracture	0.70
Total Mortality	1.01

JAMA 2004;291:1701-12

Estrogen Only: Breast Cancer

- WHI-OS
  - Lower risk of breast cancer with CEE alone (and hysterectomy)
  - < 0.625 mg CEE similar to average dose CEE (0.625 mg)
  - Transdermal E2 may confer a slightly less risk vs or conventional dose of CEE (underpowered)
  - Oral E2 vs CEE 0.625 mg = a *trend* toward higher breast cancer incidence within first 10 years of menopause; small sample size

Schufelt C, et al. Menopause 2018;(9):985

Estrogen Only: Incident and Fatal Breast Cancer

- WHI longer term data analysis and median f/u of > 20 years.

- **Estrogen alone reduced incidence of and mortality from invasive breast cancer, while combination estrogen-progestin therapy elevated incidence of but not mortality from breast cancer**.

JAMA 2020;July 28;324:369

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Estrogen Only: Breast Cancer Risk Summary - Mixed

- WHI (RCT): ET 7.2 years; ET reduced risk; reduced breast cancer mortality; cumulative 20 yr f/u
  - Jama 2020;324:369
- Smaller RCT: reduced risk
  - Menopause 2023;29(9):1086
- Nurses Health Study(observational); ET x 5-9 years; no increased risk;
  - Longer: 15 years = trend towards increase; 20 years slight increased
- Collaborative Group: ET 5-9 years=slight increased risk
  - Lancet 2019;394:1159
- Million Women's Study: ET x 5 years=35% increase breast cancer mortality (only a survey study)
  - Lancet 2019;394;1139

MHT & Breast Cancer: Mortality

- One RCT, the WHI: After 20 years of median cumulative f/u, CEE alone was associated with lower breast cancer incidence and lower breast cancer mortality compared with placebo.
- Repeat: In contrast, CEE plus MPA was associated with slightly higher breast cancer incidence but no significant difference in breast cancer mortality compared with placebo

JAMA 2020;324

WHI Summary to Date (2023)

- CEE alone significantly reduces breast cancer risk and cancer mortality.
- CEE+ MPA, when initiated in MHT naïve women, does not increase breast cancer risk and does not increase breast cancer mortality, even in women w/FH of breast cancer.
- Even if: WHI estimate of an increased risk of breast cancer is accepted, CEE + MPA would be responsible for less than 1 additional nonfatal breast cancer diagnosis for every 1,000 women treated with MHT.
- No estimate of an association between CEE and MPA and breast cancer remains statistically significant with per protocol adjustment.

Menopause J 2023;30(12):1241

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MHT & Breast Cancer: Risks in Perspective

Meta-analysis final conclusion:

- Systemic MHT most evident with estrogen-progestin with RR 1.60 during 4 years of MHT use.
- Much less with ET alone with RR 1.17.
- Vaginal estrogens - no increased risk no matter duration of 5-14 years.
- Put RR into clinical perspective and the absolute risk of an individual woman and her other risk factors:
  - **Regular alcohol** = increased risk of 32-46%
  - **Obesity** = increased risk of 26-152%
  - **Physical inactivity** = increased risk of 7-33%

ALL OF THESE ARE MUCH HIGHER THAN THE RISK CONFERRED BY MHT!!!

- Attributable Risk of Breast Cancer (CEE /MPA in WHI= less than one additional case of breast cancer diagnosed per 1,000 users annually)
- No additive effect of MHT with age or elevated personal breast cancer risk factors.
- The RR of breast cancer associated with MHT use is similar in women at average or high risk.

MHT & Breast Cancer: Genetics/FHx

- HT does not further increase the RR of breast cancer in women with FH breast cancer, in women after BSO for BRCA 1 or 2 mutations, or history of benign breast biopsy.
  - Breast Cancer Res Treat 2014;145
  - and more
- If genetic risk and < 50 y.o.: no increased risk of young onset breast cancer with use of EPT; ET alone =reduced diagnosis of young onset breast cancer.
  - Am J Epidemiol 2015;181

MHT & Breast Cancer: Type of hormone, dose, route

- Role of progestogens: OMP may have less effect on breast cancer risk vs progestins
- Type of estrogen: No difference in effects of CEE vs estradiol on occult breast cancer growth. (Collaborative Group Study)
- No difference in oral and transdermal
- Low dose vaginal estrogens- no effect
- Insufficient clinical data on CEE plus BZA

Mammograms prior to MHT

“A screening mammogram needs to be done prior to starting a patient on MHT”

- Myth.

Screening Mammograms & MHT Timing

To mammogram or not, prior to HT?

- Prudent approach: Screening mammogram in the last 1-2 years; every 1-2 years in average risk women
- No distinct consensus recommendations
- What about D/C HT for 2 months before screening mammogram???
  - Conclusions (READ study 2009)
  - Brief HT suspension was associated with small changes in breast density and did not affect recall rates. There is no evidence to support short-term HT suspension before mammography.

Screening Mammograms & Guidelines for Average Risk Women

- ACOG - Individualize at 40-49; every 1-2 yr, 50-69
- USPSTF (2023 update) - Every 2 year screening begin age 40
- WHO - Every 2 years ages- start age 40
- ACS - Ages 40 to 44: Women should be offered the choice to start annual mammograms if they wish. The risks and benefits should be considered.
  - Ages 45 to 54: Annual mammograms are recommended.
  - Ages 55 and older: Mammograms every two years are recommended. Women should be offered the choice of annual screening if they wish to have more frequent screening. Screening should continue as long as the woman is expected to live 10 years or longer.

MHT Myths

MHT Duration

“Women who take MHT should stop by the age of 60”

- Myth.

MHT Duration

Use of menopausal hormone therapy beyond age 65 years and its effects on women's health outcomes by types, routes, and doses; **Just Released 2024**

Objectives: MHT beyond 65 and health implications by types/routes/doses

Methods: Prescription drug and encounter records of 10 million senior Medicare women from 2007-2020 and Cox regression analyses

Results:

- Estrogen monotherapy beyond age 65 years was associated with significant risk reductions in mortality (19%) breast cancer (16%), lung cancer (13%), colorectal cancer (12%), CHF (5%), VTE (3%), atrial fibrillation (4%), acute MI (11%), and dementia (2%).
- Estrogen and progestogen combo-therapy, both E+ progestin and E+ progesterone: increased risk of breast cancer by 10%-19%, but such risk can be mitigated using low dose of transdermal or vaginal E+ progestin.
- E+ progestin exhibited significant risk reductions in endometrial cancer (45%) ovarian cancer (21%), IHD (5%), CHF (5%), and VTE 5%)
- E+ progesterone: risk reduction only in CHF (4%).

Conclusions: Among senior Medicare women, MHT use beyond age 65 years vary by types, routes, and strengths. Risk reductions appear to be greater with low rather than medium or high doses, vaginal or transdermal rather than oral preparations, and with E2 rather than conjugated estrogen.

Baik S, et al. Menopause J.

MHT Delivery

“Any delivery route of estrogen is safe at any age”

- Myth.

Use of Systemic Hormone Therapy After Age 65

- Weigh benefits vs risks
- Appropriate for QOL if no CIs
- Appropriate for other potential benefits if no CIs
- Lowest effective dose
- Delivery issues: Must **switch to transdermal** if on oral E

Initiation of MHT

“Postmenopausal women can safely start taking MHT at any age”

- Myth.

Therapeutic Window

- Benefits outweigh risks
- Initiate HT within 10 years to prevent:
  - Urogenital atrophy
  - Dementia (maybe even wi/5 yrs
  - Possibly cardiovascular disease
- Initiate HT within 3-6 years to prevent or treat bone loss
- **Starting MHT > 10 years after menopause or after age 60: increases risks DVT, stroke, CVD, AD**

Progesterone Cream & Endometrial Protection

“Progesterone cream is an adequate delivery method to provide endometrial protection in women who take systemic estrogen”

- Myth.

Progesterone Cream: 5 Study Details

Is it Enough for Endometrial Protection?

- 5 studies have been identified investigating the impact of transdermal micronized progesterone on the endometrium. All but one study were RCT ; some had placebo or progestin as a comparator. Sample sizes range from 27 to 54 postmenopausal women; study duration ranged from 4 weeks to 48 weeks.
- The estrogens were applied either orally or transdermally and the dosing ranges were from high end of normal dosing to moderate dose categories.
- Transdermal progesterone cream-applied either sequentially or continuously and ranged from 16 mg/day to 64 mg/day.
- One study: TVUS =significant increase in endometrial thickness.
- All five studies had an endometrial biopsy pre and post treatment.
- Two studies indicated an adequate progesterone opposing effect by the same lead author (1. **Only 28 days duration**; dose of progesterone cream was at 15 mg bid or 40 mg bid); 2. **Only 6 months duration**; 40 mg cream continuous). The 6 month study of 40 mg cream per day did have 19% of the women with proliferative endometrium, but no hyperplasia on biopsy.
- **Remaining 3 studies did not have an adequate progesterone cream opposing effect showing proliferative endometrium and two cases of complex hyperplasia but no endometrial cancer.**
- One of the negative studies, the one with complex hyperplasias were 48 weeks duration; two of the negative studies were 12 weeks duration.

Progesterone Cream vs Progestins and Endometrium; 1 of the 5

Objective: To evaluate the endometrial effects and determine patients' acceptance of transdermal progesterone cream compared to standard hormone therapy.

Methods: Healthy menopausal women-pretreatment endometrial biopsy (EMB). Randomized to 0.625 mg conjugated equine estrogen (CEE) daily and 2.5 mg medroxyprogesterone acetate (MPA) (Prempro) or daily 0.625 mg CEE and twice daily **20 mg transdermal** PC. At the end of **6 months**, a repeat EMB was obtained, and the women were crossed over to other treatment. A final EMB was performed after the final 6 months.

Results: Twenty-six women completed both arms of the study. Seventy-seven percent of women preferred the CEE/PC to the CEE/MPA . Of the 52 post-treatment endometrial biopsies: 40 revealed atrophic endometrium and 12 proliferative endometrium (7 in the oral progestin group and 5 in the PC group). There was no evidence of endometrial hyperplasia in any of the specimens. The incidence of vaginal spotting was similar in both groups.

Problems: Too small, Too short to determine safety of progesterone cream- at least in this dose

Altern Ther Health Med . Nov-Dec 2005;11(6):36-8.

Progesterone Cream: Endometrium Insufficient Anti-proliferative Effect

- In general, these studies
  - too short
  - too few/too small
- Concerning cases of endometrial thickening, hyperplasia and complex hyperplasia, even in these short durations.
- Endometriums being stimulated by systemic estrogen with unopposed progestogens in women with a uterus tend to get thicker, more proliferative and more hyperplastic with increased risk of atypia and cancer over time
- **Need: Specific doses, forms and deliveries of progestogens that are accepted methods of providing adequate endometrial protection, based on adequate studies.**

Progestogens: Endometrium

- Dose and delivery of progestogens required for endometrial opposition is dependent on the background estrogen dose (ave = 0.625 mg oral CEE; 1 mg oral E2; 0.05 mg td)
- Half average = 0.3 CEE; .5 oral E2; 0.025 td
- Continuous vs 12-14 days/month/vs IUD
- Typical Doses in Clinical Trials:

	Cyclic	Continuous
MPA	5-10 mg/day x 12-14 days	1.5-2.5 mg/day
OMP	200 mg/day x 12-14 days	100 mg/day
Vaginal P gel	45mg/day >10d/mo	100 mg cap/day every other day
Norethindrone acetate		0.5-1mg/day
Drosperinone		0.5 mg/day
Combi-patches		LNG10-40 mcg/day; NETA
LNG-IUD*		20 mcg/day; 10 mcg/day (no hyperplasia at one year

*LNG IUD is released at a rate of approximately 20 mcg/day. This rate decreases progressively to approximately 10 mcg/day after 5 years and 9 mcg/day after 6 years.

Other Myths

“Women with a history of breast cancer cannot use vulvovaginal estrogen for GSH”

“Progestins and Progesterone have the same effect of the breast”

- Myths.

2020 Genitourinary Syndrome of Menopause Position Statement-NAMS

- Education and screening for GSM
- First line therapies: non hormone lubricants with sexual activity and regular use of long-acting vaginal moisturizers
- Moderate to severe GSM and non responders to lubricants and moisturizers:
  - 1. Low dose vaginal ET 2. Vaginal DHEA 3. Ospemifene 4. Systemic ET (when VMS are also present)
- If history of breast or endometrial cancer: consider woman's preferences, symptom severity and understanding of potential risks after consultation with her oncologist
- VET risks not the same as systemic ET Although label is not helpful
- Progestogen not recommended with low dose VET; if increased risk of endometrial cancer may warrant endometrial surveillance.
- Routine endometrial surveillance not recommended for asymptomatic women using low dose vaginal ET. Consider TVUS or intermittent Progestogens for women at increased risk of endometrial cancer.
- Spotting or bleeding in a postmenopausal woman: requires a thorough evaluation
- Vaginal laser/radio frequency devices requite long term, sham-controlled safety and efficacy studies before their routine use can be recommended
- Therapy for GSM should be continued, with appropriate clinical f/u for as long as bothersome symptoms are present; symptoms likely recur if VET is d/c

French Study #1

Progesterone may increase breast cancer risk less than progestin

- The risk of breast cancer is slightly increased with a postmenopausal hormone therapy regimen consisting largely of transdermal estradiol combined with progestins, but not when combined with progesterone.

Int J Cancer 2005;114:448-454.

French Study #2

Unequal risks for breast cancer associated with different HT

- Data from the French E3N cohort study
- 2,354 cases of invasive breast cancer among 80,377 postmenopausal women over 8 years.

E alone	1.29 (1.02-1.65)
E-Progesterone	1.00 (0.83-1.22)
E-dydrogesterone	1.16 (0.94-1.43)
E-other progestins	1.69 (1.50-1.91)

Fournier, et al. Breast Cancer Res Treat 2008;107(1):103-111

French Study #3

Role of Progestogen Type in Breast Cancer Risk

- The type of progestogen and regimen used affect breast cancer risk.
- Breast cancer cases (739) and matched controls (816) with no breast cancer history.
- OMP: Breast cancer risk was not increased.
- The odds of breast cancer for users of progesterone-derived progestogens (progestins) were 1.5 times higher than in controls, and the odds for users of testosterone-derived progestogens were 3.35 times higher than for controls.
- Women who used continuous combined regimens were at higher risk than those who used sequential regimens, but most were testosterone-derived progestins.
- In addition, women who start HT early after the onset of menopause were at higher risk of breast cancer than women who delayed treatment for 1 or more years. (this is an outlier finding)

PLoS One 2013;8(11)::e78016

UK Study

MHT Formulation - Breast Cancer Risk

- Population based case control study of women aged 50 years or older; UK
- Over about 20 years: 43,183 cases of breast cancer identified and matched to 431,830 women in control group.
- EPT use vs never used: very slight increased risk of BC
- ET alone use vs never used: not associated with BC
  - Bio-identical estrogens 1.04
  - Animal-derived estrogens 1.01
  - Both 0.96
- Progestogens were differentially associated with breast cancer; (micronized progesterone (R 0.99) synthetic progestin OR 1.28

Obstet Gynecol 2022;139(6):1103

Fournier (observational study)

Endometrial CA; E + OMP

- Mean f/u of 10.8 years.
- Compared with never use, E + OMP (ave of 22.5 days/month) (OMP 100 mg/day or 200 mg 12 days/mon) was associated with an increased risk of endometrial cancer and HR of 1.8
- And was significantly more marked with longer duration : 5 or less years = 1.39 and > 5 years = 2.66

Fournier A. A J Epidemiology 2014; 180 (5)

Dr. Hudson Resources

- *Women's Encyclopedia of Natural Medicine;*
  2nd Edition 2008; Hudson; McGraw-Hill
- The Menopause Companion, Roost Books 2023
- www.drtorihudson.com
- www.instituteofwomenshealth.com
- www.awomanstime.com

Thank You!

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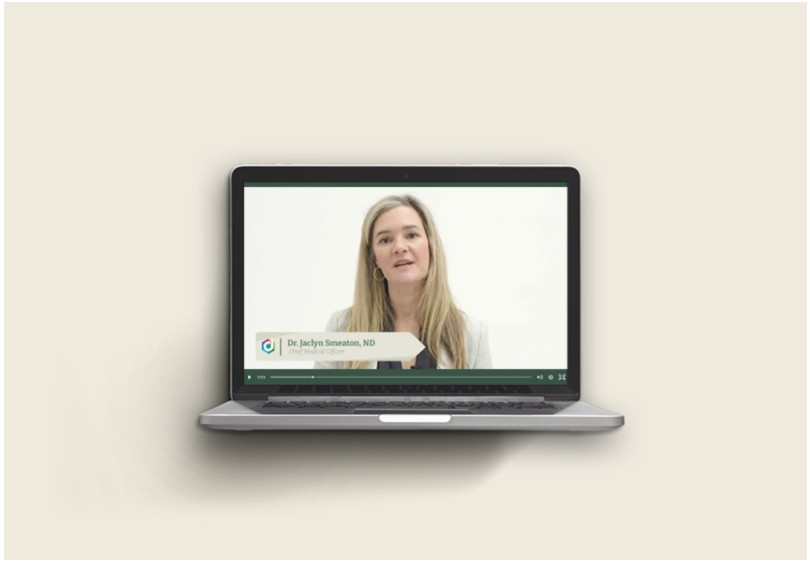

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