



Menopause Management for the Rural Physician

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I can't wait for menopause.

...said no one ever.



your  cards
someecards.com

Disclosures

- ▶ I did not receive pharmaceutical funding for this lecture
- ▶ I confirm that I had full editorial control over the content of this presentation and wish to advise that it may contain content that is not consistent with the approved Canadian Product Monographs
- ▶ I am involved in the speakers bureau and/or Advisory boards of Bayer, Duchesnay, Biosyent, Lupin, Astellas, Eisai, Searchlight, Abcellera, Knight, and Pfizer.



35 minutes is not a long
time...but menopause is!

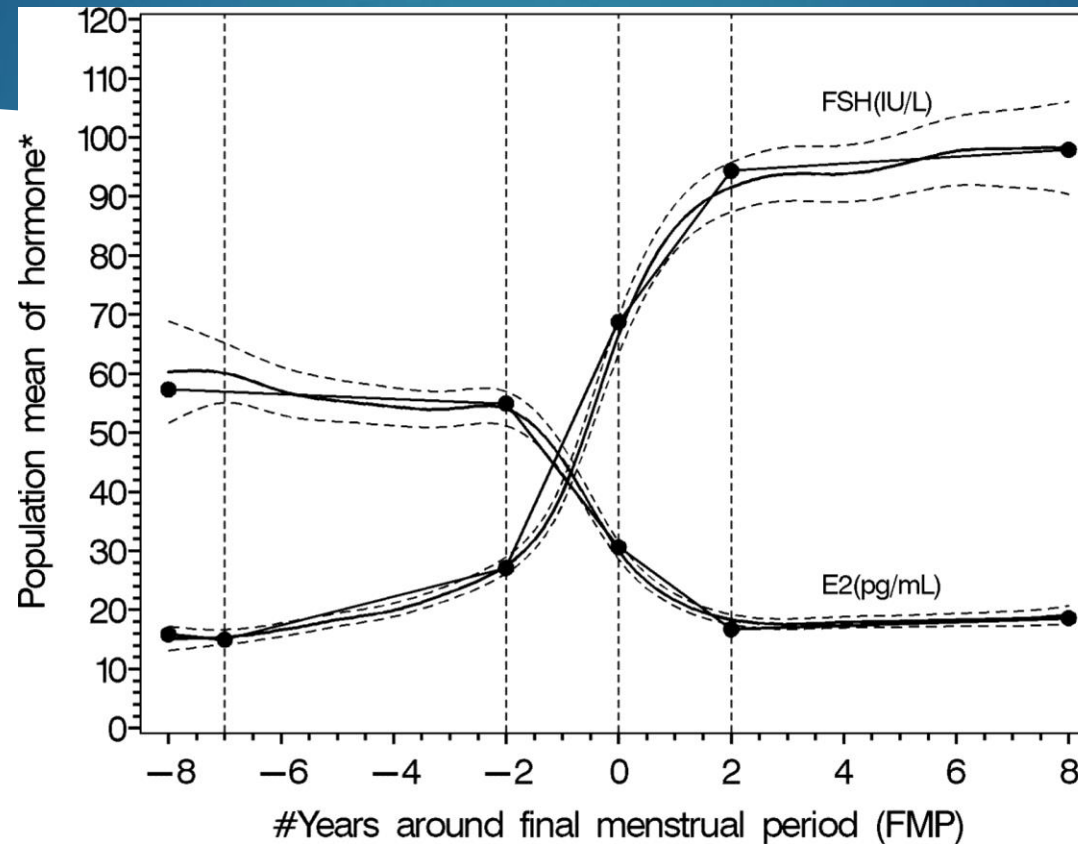
What is spontaneous menopause?

- ▶ A normal and natural event
- ▶ Marked from 1 year after final menstrual period (FMP)
 - ▶ Only a retrospective diagnosis
- ▶ Results from a loss of ovarian follicular function
- ▶ Average age 51.4 years (in North America)
- ▶ Women now expect to live 1/3-1/2 of our lives in menopause

What is menopause?

- ▶ May also occur prematurely due to iatrogenic causes (bilateral oophorectomy, chemotherapy, radiation)
- ▶ At any time from impaired ovarian function due to other causes
 - ▶ Idiopathic
 - ▶ Autoimmune disease
 - ▶ Genetic causes

Changes in estradiol and FSH during menopause transition (SWAN)





Menopause can have a
myriad of different
presentations....

The Hallmark of Menopause

Vasomotor Symptoms (VMS):

- ▶ Hot flushes and night sweats affect 75-80% of peri/postmenopausal women
- ▶ VMS have been associated with:
 - ▶ Poorer health condition or poorer health status
 - ▶ Reduced work productivity
 - ▶ Impaired quality of life
 - ▶ A possible cardiac marker



TRACKING



3:56am
4:30am

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		? → 8:00am	1:18 am		
		9:00am	2:57am		
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		3:28 pm	9:01am		
		4:05 pm	10:12am (10)		
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Menopause = More Than Hot Flashes

Common menopause related symptoms	Other symptoms associated with menopause	
<ul style="list-style-type: none">• Hot flashes and night sweats• Vaginal dryness• Irregular menses	<ul style="list-style-type: none">• Mood changes• Cognition disturbances• Sleep disturbances• Stiffness/soreness/joint pain• Weight gain• Fatigue• Palpitations• Forgetfulness• Headaches, migraines, backaches• Breast symptoms*	<ul style="list-style-type: none">• Irritability• Recurrent urinary tract infections• Urinary urgency and/or incontinence• Anxiety• Depression not responsive to antidepressants• Loss of libido

*Breast tenderness decreases in late perimenopause/postmenopause vs. before and in early perimenopause.



Hormone therapy is the
gold standard for
vasomotor symptom
treatment

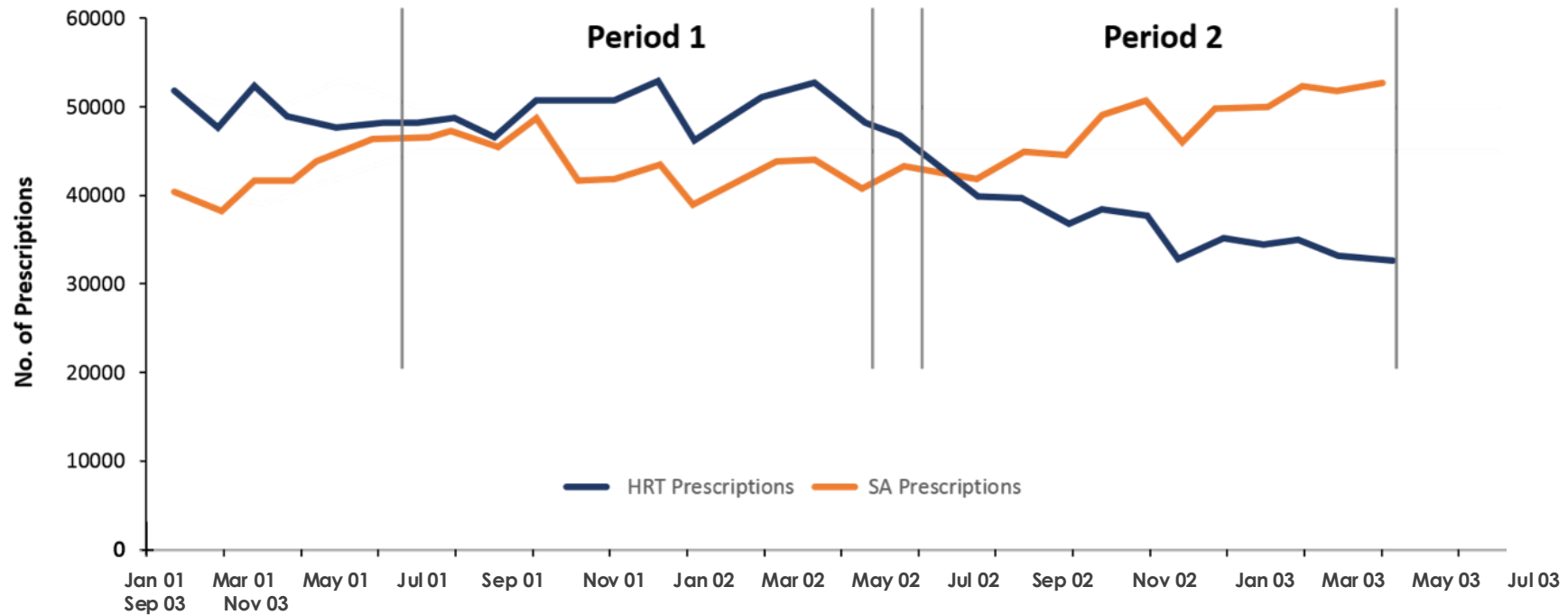
2022 Menopause Society Hormone Therapy Position Statement

- ▶ HT is the most effective treatment for VMS and has been shown to prevent bone loss and fracture
- ▶ Benefits are mostly likely to outweigh risks for symptomatic women who initiate HT when aged <60 years or who are within 10 years of menopause onset



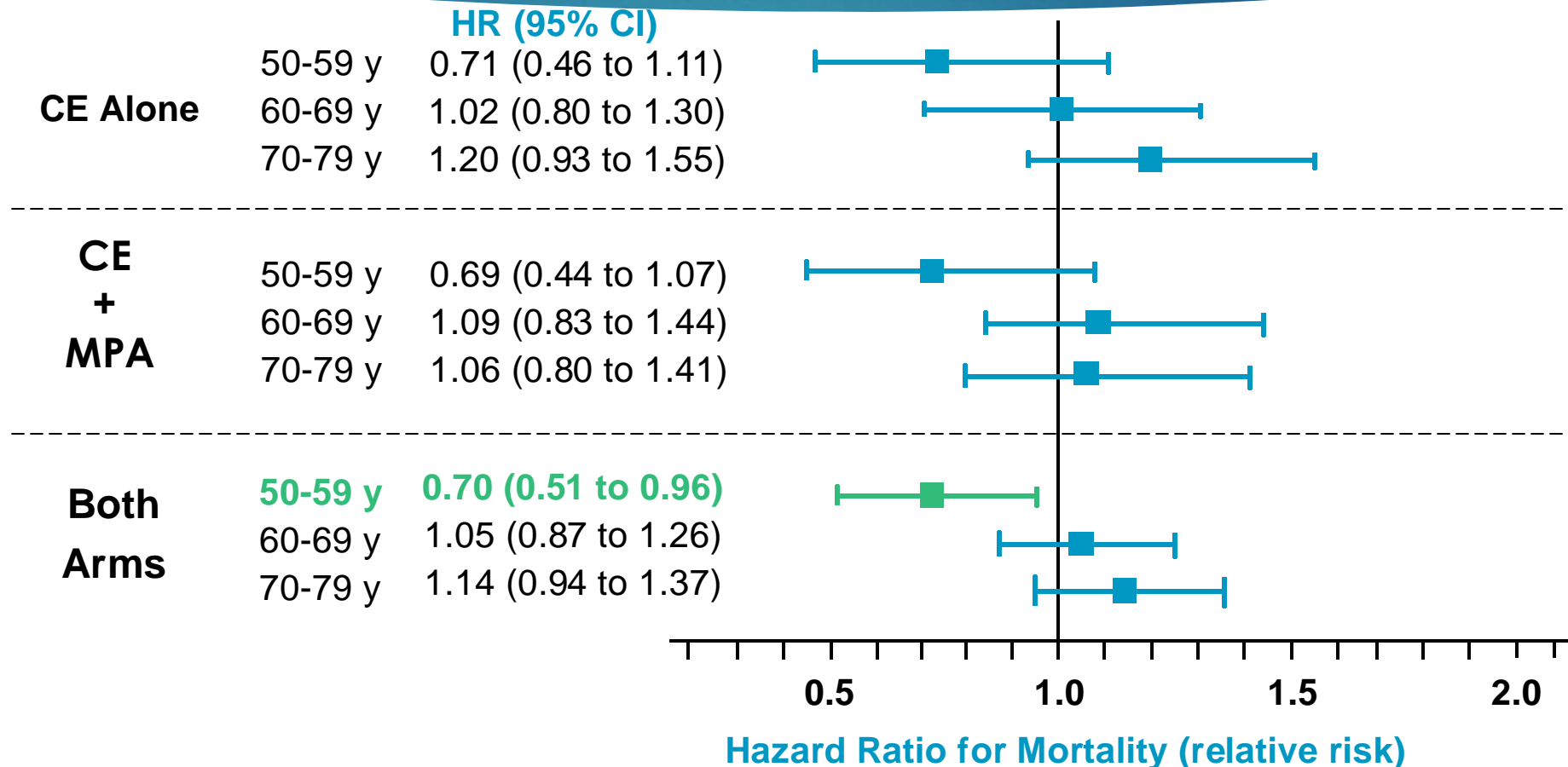
The
**Menopause
Society™**

The WHI Aftermath



1. McIntyre et al. *CMAJ* 2005;172 (1):57-59;
2. Pinkerton & Santoro. *Menopause* 2015;22(9):926-36.

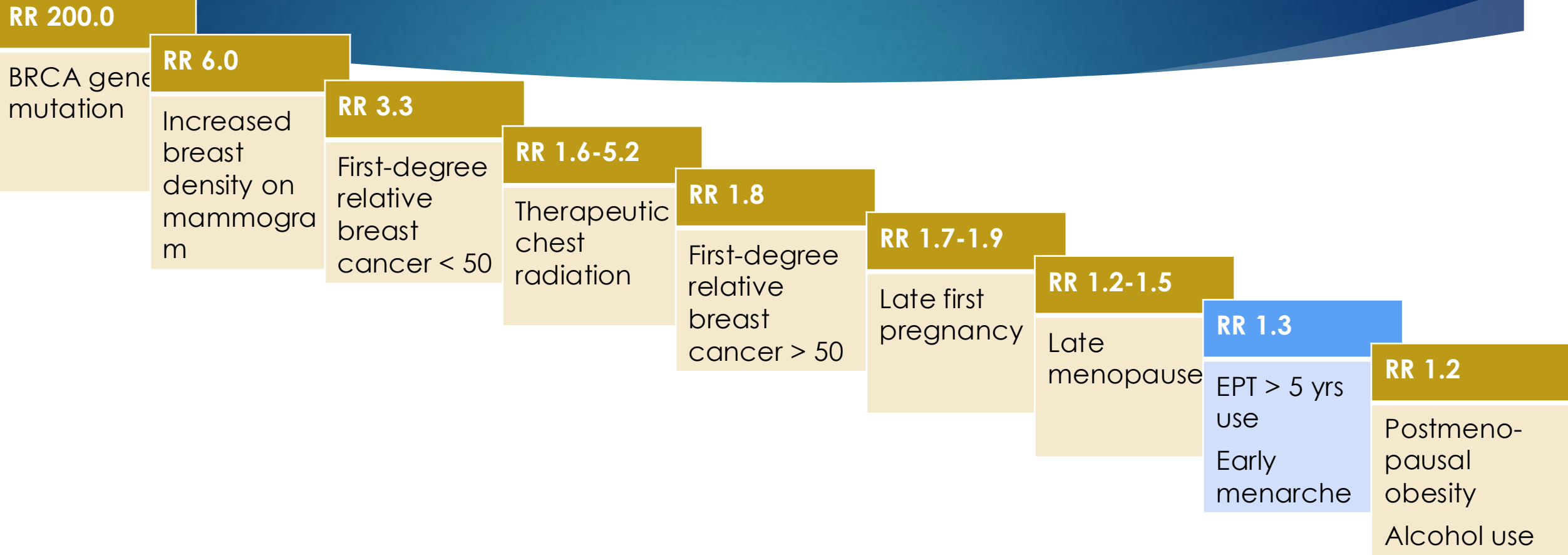
Evidence For the “Timing Hypothesis”: WHI: Total CV Mortality by Age





Breast cancer is common

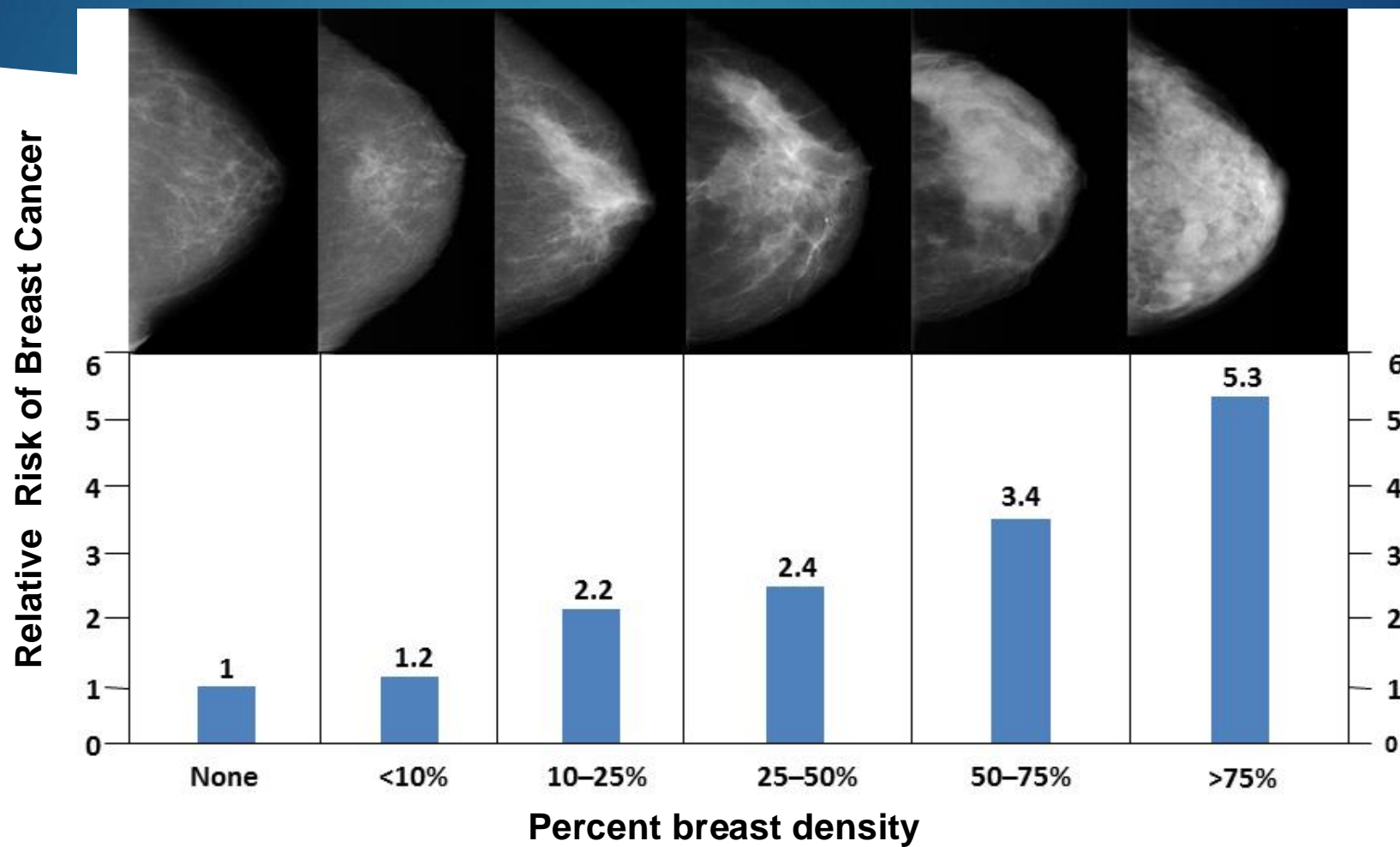
Multifactorial Risk Model for Breast Cancer




RR: relative risk

Singletary SE. Ann Surg 2003; 237(4):474-82

Breast Density and Relative Risk of Breast Cancer





Most people are
candidates for hormone
therapy!

Hormone Therapy

Contraindications to HT	Relative contraindications to HT
<ul style="list-style-type: none">• Unexplained/undiagnosed vaginal bleeding prior to investigation• Known or suspected breast carcinoma• Acute liver disease• Active thromboembolic disease• Acute cardiovascular disease• Recent stroke• Pregnancy	<ul style="list-style-type: none">• Smoking• Diabetes• Hypertension• Migraine



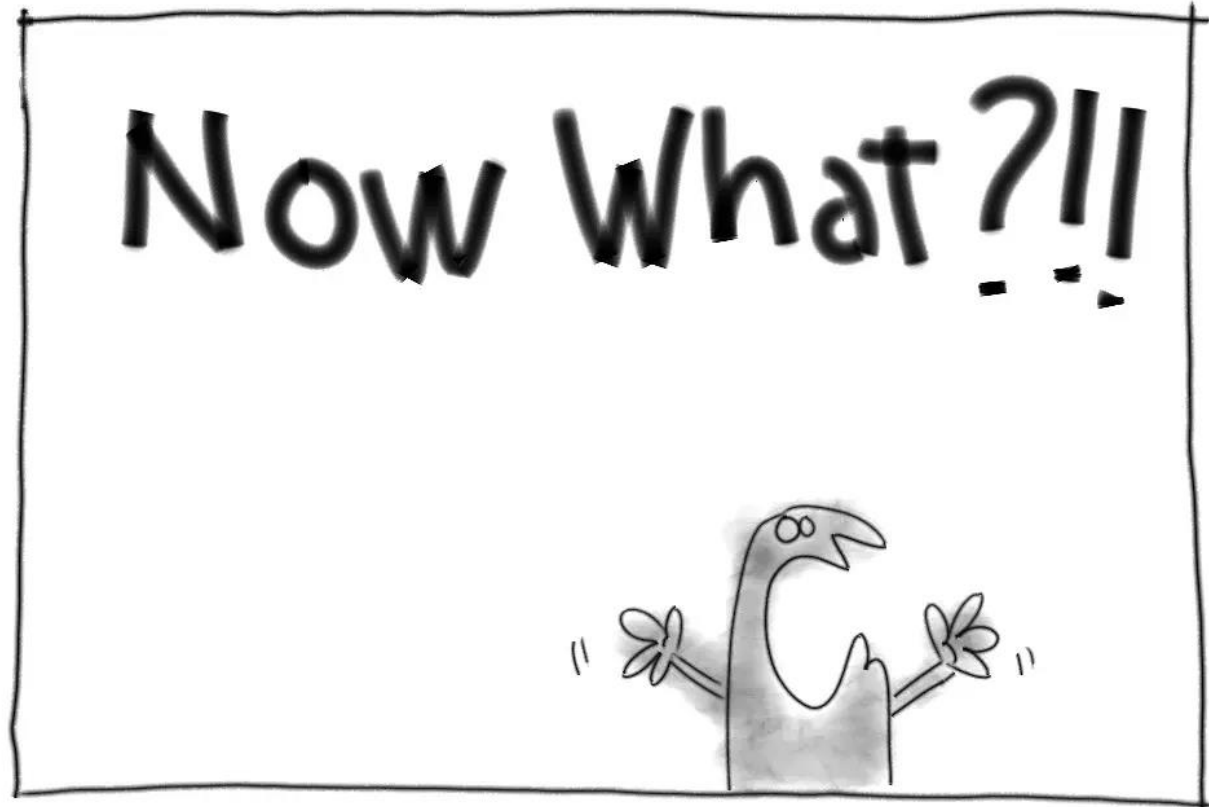
If you're not sure how to
prescribe MHT.....

Pick one of these and try it!

- ▶ 17b Estradiol gel 1-2 pumps OD transdermally + micronized progesterone 100 mg PO OD
- ▶ 17b estradiol patch 37.5-50 mcg change twice weekly + micronized progesterone 100 mg PO OD
- ▶ Estradiol 1mg PO OD + micronized progesterone 100 mg PO OD
- ▶ Combined oral pill (1 mg estradiol plus 1 mg drospirenone) 1 tab PO OD
- ▶ CEE 0.625 mg PO OD + MPA 2.5 mg PO OD
- ▶ Combined CEE and bazedoxifene 1 tab PO OD
- ▶ Tibolone 1 tab PO OD
- ▶ 17b Estradiol gel .5mg daily + Progestin

- ▶ Progestogen equivalencies:
 - ▶ MPA 2.5mg OD = micronized progesterone 100mg OD
 - ▶ The LNG IUS (52mg) can be used as a progestin in any of these regimens

So you've written a prescription for
MHT....



You've written a prescription....

- ▶ Follow-up in 4 months to assess success with treatment
- ▶ Advise bleeding/spotting can occur with any stop/start/skip/change of HT
- ▶ Reassess annually and consider trial off if not needed any more
 - ▶ Can stop cold turkey or taper
- ▶ Ensure pap tests, mammography (q2 years) and FITT screening are up to date



What if they bleed?!?!

Abnormal Bleeding on MHT

- ▶ One of the most common side effects
 - ▶ 40% of women will bleed on continuous combined MHT
 - ▶ Bleeding is expected if women are using short or long cycle MHT
- ▶ Increased chance of bleeding if MHT started within 12 months of FMP
 - ▶ Consider cyclic or IUS progestin for peri/newly menopausal women to reduce AUB
- ▶ MHT does not increase risk of endometrial disease
 - ▶ Unopposed estrogen does

Abnormal Bleeding on MHT

- ▶ Most bleeding resolves within 6 months of initiation of MHT
- ▶ Bleeding lasting longer than 6 months should be investigated
- ▶ Bleeding in women with risk factors should be investigated immediately
 - ▶ **Increased BMI**
 - ▶ History of endometrial hyperplasia
 - ▶ Family history of hereditary mutation (eg. Lynch Syndrome)
 - ▶ History of prolonged anovulation
 - ▶ Tamoxifen use
 - ▶ Unopposed estrogen use

Abnormal Bleeding on MHT

- ▶ Investigation of bleeding
 - ▶ Comprehensive history
 - ▶ ****PHYSICAL EXAMINATION WITH SPECULUM****
 - ▶ Swabs, inspection of cervix, pap test if required
 - ▶ Bimanual exam
 - ▶ Endovaginal pelvic ultrasound
 - ▶ *Pearl – counsel your patients WHY you have ordered an EVUS.... They are less likely to decline it at the ultrasound facility!*

Abnormal Bleeding on MHT

- ▶ If EVUS shows endometrial disease → Biopsy
- ▶ If EVUS shows endometrial pathology (polyp, fibroid) → Hysteroscopy
- ▶ If EVUS shows lining ≤ 5 mm → Surveillance
- ▶ If EVUS shows lining ≥ 5 mm → Biopsy

- ▶ For all menopausal women, an endometrial lining ≤ 4 mm = 1/917 chance of endometrial cancer and biopsy is not recommended

- ▶ Caveat: ongoing, heavy bleeding with risk factors

Abnormal Bleeding on MHT

- ▶ So how do I fix it??
- ▶ Does your biopsy or physical exam help you?
 - ▶ Atrophic endometrium or lower tract
 - ▶ Proliferative/weakly proliferative
 - ▶ Hyperplasia/malignancy/polyp → Refer
- ▶ Can always take a break and await resolution
- ▶ Consider LNG-IUS and add estrogen on top
 - ▶ Prefer 52mg and leave for 5 years... more?

Abnormal Bleeding on MHT

- ▶ Anecdotally, some preparations have better bleeding profiles than combined regimens
 - ▶ TSEC (CEE + bazedoxifene)
 - ▶ Tibolone
 - ▶ Combined products
 - ▶ Eg. 1mg estradiol + 1mg Drospirenone PO OD
 - ▶ Eg. 1mg estradiol and 0.5mg NETA PO OD
- ▶ Definitive surgical management has been done....



No maximum length of use

Duration of hormone therapy use

- ▶ With EPT, increased risk of breast cancer incidence with 5 years of use
 - ▶ 8/10,000 users per year
- ▶ With ET, no increase of breast cancer with early postmenopausal use
- ▶ Extending EPT use is acceptable for:
 - ▶ Women who request it and are counselled
 - ▶ Prevention of osteoporosis for women at high risk of osteoporotic fracture when alternate therapies are not appropriate
- ▶ Decision to continue HT should be **individualized**



Sometimes A Hot Flash Is
Not A Hot Flash

What Else Can Cause a “Hot Flash”

- ▶ Thyroid disease
- ▶ Infection
- ▶ Leukemia
- ▶ Diabetes
- ▶ Adrenal tumors
- ▶ Autoimmune disorders
- ▶ Anxiety
- ▶ Central Sensitization Syndrome
- ▶ Drugs: SERMs, SSRIs, aromatase inhibitors

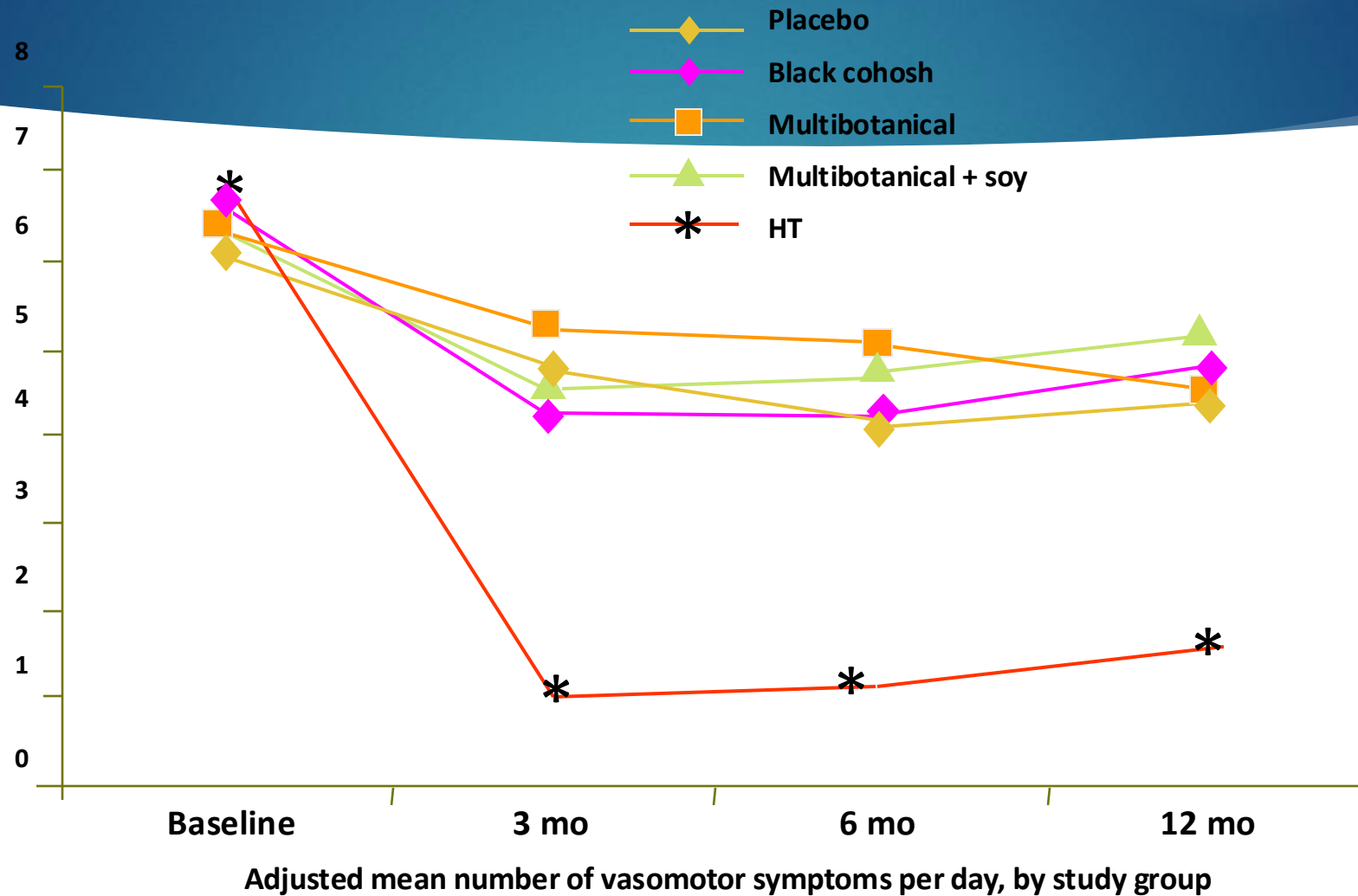


Breast cancer survivors
are not candidates for
systemic hormone
therapy



Herbs don't help

Efficacy of HT vs. Herbals, Soy and Botanicals





Some non-hormonal
medications can help!

Non hormonal treatment of vasomotor symptoms

MS Guideline 2023

- **SSRI/SNRI** are associated with mild to moderate improvements in VMS
 - Paroxetine salt 7.5mg is on-label in USA
 - Citalopram, escitalopram, desvenlafaxine, venlafaxine
 - Avoid Paroxetine on tamoxifen
 - Low dose therapy
 - Co-treat for depression/anxiety
- **Gabapentin** is associated with improvements
 - Start slow and low (100mg→2400mg); 900mg is most effective dose for VMS
 - AEs: somnolence, dizziness – typically improve
- **Oxybutynin** has been shown to be useful
 - In older adults, long-term use can be associated with cognitive decline (so have VMS!)
 - Start at 2.5→5mg BID (use to cover OAB symptoms as well)
 - AEs: dry mouth, urinary retention, constipation

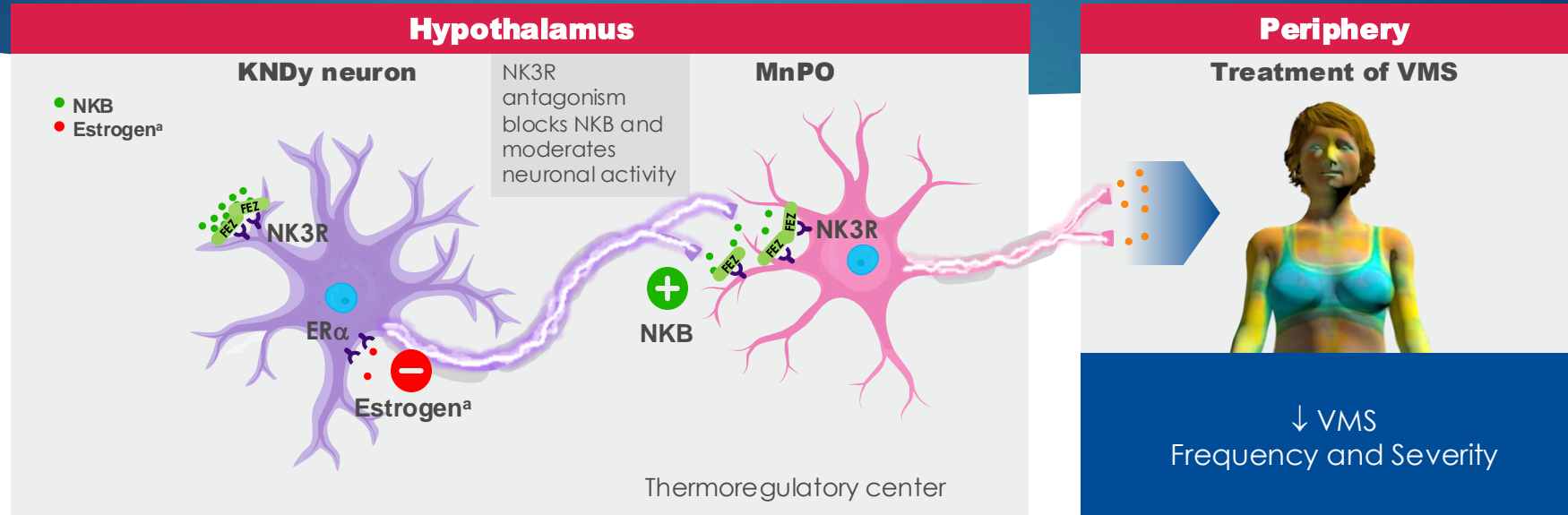
No longer recommended

Pregabalin (adverse effects – weight gain and also a controlled substance with prescribing restrictions and possible dependency)

Clonidine (adverse effects and poor evidence) are not recommended

Coming Soon.....

Neurokinin B antagonists!



Fezolinetant is a selective NK3R antagonist that blocks NKB binding on the KNDy neuron to moderate neuronal activity in the thermoregulatory center, **helping to restore thermoregulatory balance**¹⁻⁵






ER α , estrogen receptor alpha; FEZ, fezolinetant; KNDy, kisspeptin-neurokinin B-dynorphin; MnPO, median preoptic nucleus; MOA, mechanism of action; NK3R, neurokinin 3 receptors; NKB, neurokinin B; VMS, vasomotor symptoms.
Figure adapted from Depypere H, et al. *Expert Opin Investig Drugs*. 2021; 30: 681-694. 2. Hoveyda HR, et al. *ACS Med Chem Lett*. 2015; 6: 736-740. 3. Depypere H, et al. *J Clin Endocrinol Metab*. 2019; 104: 5893-5905. 4. Fraser GL, et al. *Menopause*. 2020; 27: 382-392. 5. Tahara A, et al. *Eur J Pharmacol*. 2021; 905: 174207.

^aAvailable data support an inhibitory effect of estradiol, specifically, on KNDy neurons.




What about vaginal
dryness, painful sex and
vulvar pain in menopause?

GSM Hormonal Treatment Options

Hormonal options				
Low-dose vaginal estrogen			Selective estrogen receptor modulator	Vaginal DHEA
Creams	Inserts	Ring		
				
Conjugated estrogen .5-1g PV QHS x 2 weeks then 2x/week Estrone	17β estradiol soft gel 4 or 10ug 17β estradiol suppository 10ug PV QHS x 2 weeks then twice weekly	17β estradiol q3months	Ospemifene **oral** 1 tab PO OD	Prasterone 1 supp PV QHS

****No Progestins Required!****

The NAMS 2020 GSM Position Statement Editorial Panel. *Menopause*. 2020;27(9):976-992; Johnston S, et al. *J Obstet Gynaecol Can*. 2021;43(11):1301-1307.e1; Lim J, Uzelac A, Christakis M, Shirref L. The Genitourinary Syndrome of Menopause. Gynaecology Quality Improvement Collaboration: v03.08.2023 <https://gynqi.com/wp-content/uploads/2023/04/M3-Genitourinary-Syndrome-Menopause-v03.08.2023.pdf>



So which Instagram
menopause vitamins
should I buy...?

Do I need hormone balancing?

Am I estrogen dominant?

What is the key to a healthy
menopause?

How to have a healthy menopause!

- ▶ Move your body outside every day
 - ▶ **Target 150min moderate intensity exercise/week and weight/strength training 3 days per week**
- ▶ Follow cervical screening guidelines until age 69
- ▶ Follow breast screening guidelines
 - ▶ Can self refer!
- ▶ Have a routine bone density at age 70 (or earlier if risk factors)
- ▶ Follow colon cancer screening guidelines
- ▶ Consider a meditation and/or gratitude practice
- ▶ Institute measures to prevent falls and improve balance/core strength
- ▶ Get good sleep and have good sleep hygiene

Specific dietary recommendations

- ▶ Eat a balanced diet, prioritize protein, and consider portion control
 - ▶ Dietary control of blood sugar and cholesterol
- ▶ Obtain adequate calcium and vitamin D
 - ▶ Calcium: 1,500 mg/d from food (preferably) and/or supplement
- ▶ Abstain from smoking and alcohol altogether
- ▶ Avoid late night snacking (brush teeth after dinner)
- ▶ Target 25-30mg of fibre per day (up to 90% of women are fibre-deficient)
- ▶ Target .8-1.2g/kg body weight/day in protein
- ▶ Prioritize legumes/beans/lentils/chick-peas/soy for fibre/protein
- ▶ Abstain from processed foods (“things with an ingredient list” and saturated fats)
- ▶ Maintain hydration (8 cups per day – prefer clear tea, water)

The Pearls!

- ▶ Don't ask? Won't tell.... Sexual function.... VMS.... Sleep.... Bladder
- ▶ Almost EVERYONE benefits from a local vaginal hormone
 - ▶ Think about post-partum patients too!
- ▶ Hormone therapy is **safe** and the gold standard
 - ▶ Pick a few options and try people.... They will thank you!
- ▶ Don't remove LNG-IUDs – you can use them as part of MHT!
- ▶ Counsel and screen for breast cancer

The Pearls!

- ▶ Tibolone, estrogen alone (if hysterectomized) and the TSEC are not associated with increased risks of breast cancer and are the **best choices** for women with dense breasts
- ▶ Breast cancer survivors can be candidates for GSM treatment:
 - ▶ Prefer Vaginal Prasterone (if on AIs or Tamoxifen) or ospemiphene (if treatment is complete)
- ▶ No maximum length of duration! Trial off and reassess
- ▶ TD estrogen = no increased risk of clot or CAD under age 60 for healthy women

Resources for Health Care Providers

- ▶ ****www.victoriaobgyn.com **** → Healthy Library
- ▶ Pathways
 - ▶ www.mq6.ca
 - ▶ Treatment algorithm
 - ▶ RACE line
- ▶ www.menopauseandyou.ca
- ▶ www.menopause.org
- ▶ www.sigmamenopause.com



A photograph of a wooden boardwalk path winding through a dense, mossy forest. The path is made of dark wooden planks and is flanked by lush green ferns and moss-covered ground. Large, gnarled tree trunks are visible on either side, and the background is filled with more trees, creating a sense of depth and a misty atmosphere. The word "Questions?" is overlaid in white text in the center of the image.

Questions?