



**What are my options?**  
**NONHORMONE AND HORMONE MANAGEMENT OF VASOMOTOR SYMPTOMS**

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**Disclosures**

Relevant Disclosures:  
 The Menopause Society Board of Directors  
 Consultant: Astellas  
 No conflicts of interest

References:  
*I will discuss clinical studies of off label use of pharmaceuticals for vasomotor symptoms.*  
*This presentation references people born with ovaries. I may use the terms women, she, and her. These terms may not capture the diversity of all those experiencing menopause. We need more research to explore how diverse people experience menopause.*

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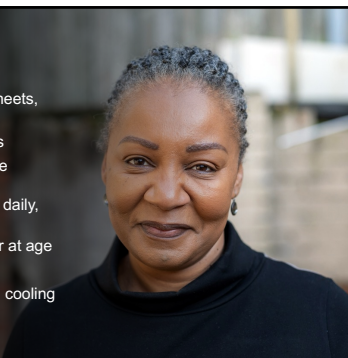
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**59 years old**

LMP: age 52  
 Symptoms: night sweats, soaks bedsheets, disrupted sleep  
 Gyn hx: sexually active, some dryness  
 PMH: HTN, well managed with lifestyle changes, previously used Amlodipine  
 Social: denies tobacco use, exercises daily, strength training 3x per week  
 Fam Hx: Mother dx with Breast cancer at age  
 Allergies: Black cohosh  
 Treatment: Exercise, dietary changes, cooling bed linens, bedside fan  
 "I want a natural treatment..."

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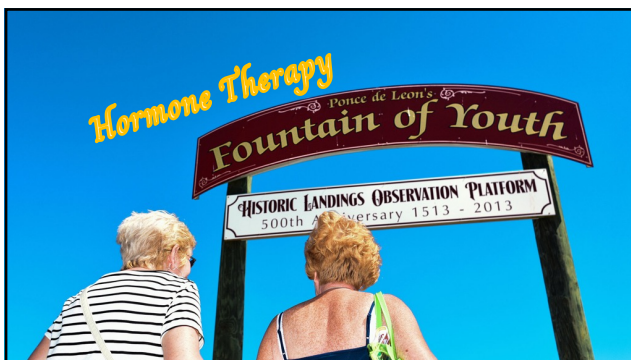
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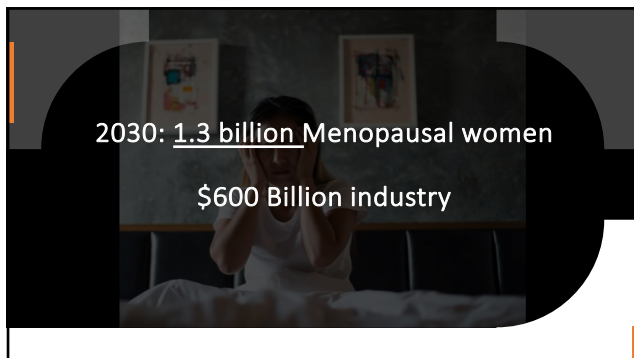
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### Vasomotor Symptoms (VMS)

- Mild: sensation of heat without sweating
- Moderate: sensation of heat with sweating, able to continue activity
- Severe: sensation of heat with sweating, causing cessation of activity

The diagram illustrates four stages of vasomotor symptoms using human figures and thermometers. Stage 1 shows a normal state with a thermometer at a baseline level. Stage 2 shows a thermometer rising, indicating a peak in core body temperature, skin blood flow, and heart rate. Stage 3 shows a thermometer at its highest point, representing an intense feeling of heat and redlining of the upper body. Stage 4 shows a thermometer falling, indicating a heart rate peak, skin blood flow peak, sweating, and the onset of chills and shivering.

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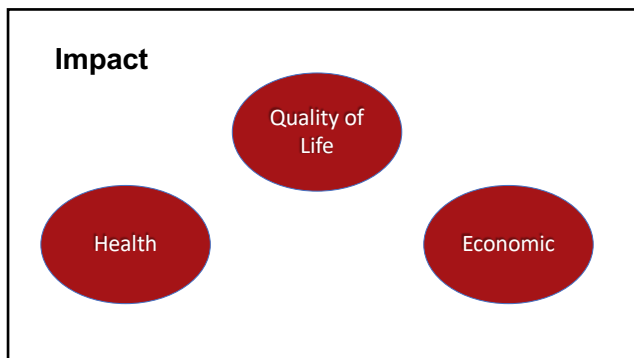
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### Duration of Hot Flashes

Shorter	Longer	Median Years
Postmenopause with symptom onset	Pre/perimenopause at symptom onset	3.4 v 11.8
Japanese/Chinese	African American race	4.8/5.4 vs 10.1
Non-Hispanic White	Hispanic	6.5 v 8.9
Education ≥ College	Education < College	7.7 v 9.9
Stress never/almost never	Stress at least sometimes	8.9 v 10.8
No depression	Depression	7.7 v 11.0
No anxiety	Anxiety (mild-severe)	5.0 v 7.4
	Financial strain	
	Poor social support	
	Obesity	
	Smoking	
	Single	

Gold EB, et al. Am J Epidemiol. 2000;152(5):463-473; Thurston NC, et al. Obstet Gynecol Clin North Am. 2011;38(3):489-501; Shobeiri F, et al. J Menopausal Med. 2016;22(1):78-85; Wilson LS, et al. Menopause. 2016;9(1):1-7; Herber-Gast GC, et al. Am J Clin Nutr. 2013;97(5):1092-1099.

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### Treatment Options

**Hormone**

- Estrogen
- Estrogen + Progesterone
- Estrogen + SERM

**Non-hormone**

- Pharmaceutical therapies
- Behavioral and lifestyle changes
- Dietary supplements

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### Estrogen



FDA APPROVED: 1<sup>ST</sup> LINE THERAPY FOR VMS

REDUCES VMS FREQUENCY, INTENSITY



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## Non-Oral Estrogen Therapy





Transdermal/Topical/Vaginal

- Patch, gel, spray, and emulsion
- Avoids first-pass hepatic metabolism
- More stable serum levels
- Minimal effect on SHBG; minimized negative impact to sexual function
- Reduced risk of VTE/stroke compared to oral ET in observational studies

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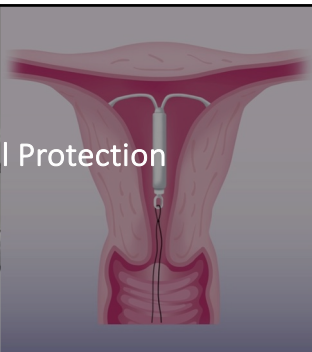
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## Endometrial Protection

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## Types of Progestogen Therapy

Micronized Progesterone

- Compound identical to endogenous progesterone
- Prometrium is the only FDA-approved bioidentical progestogen
- Contraindicated in women with peanut allergy
- Bedtime dosing advised because of sedating effects

Progestin

- Synthetic products with progesterone-like activity
  - Medroxyprogesterone acetate (MPA) is the most commonly used and studied in the United States for endometrial protection
  - Norethindrone aceta (NETA)

Schussler P, et al. Psychoneuroendocrinology. 2008;33(8):1124-1131. Montplaisir J, et al. Menopause. 2001;8(1):10-16.

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### Methods of EPT Administration

Continuous-cyclic (sequential)

- Daily estrogen with progestogen added cyclically for 12-14 d each month
- 80% of women will experience bleeding with progestogen withdrawal

Continuous-combined

- Daily estrogen and progestogen
- Low rates of endometrial hyperplasia
- Higher rates of amenorrhea
- Decreased breakthrough bleeding after 2 yrs

Ettinger B, et al. *Obstet Gynecol*. 1984;63(5Pt1):693-700. Ettinger B, et al. *Obstet Gynecol*. 2001;98(2):205-211. Olsmark IS, et al. *Menopause*. 2005;12(6):699-707. Sterow AC, et al. *Obstet Gynecol*. 2007;109(3):581-587. Prempro [package insert]. Philadelphia, PA: Wyeth; 2009. Furness S, et al. *Cochrane Database Syst Rev*. 2012;(8):CD000402. Casper RF, et al. *J Soc Gynecol Invest*. 1996;3(5):225-234.

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### Alternative Progestogen Options

- Levonorgestrel-containing IUD
- May provide endometrial cancer protection
- Off label
- Long-term efficacy data is needed

Warren MP, et al. *Am J Obstet Gynecol*. 1999;180(1 pt 1):42-48. Luo L, et al. *Cochrane Database Syst Rev*. 2018;12:CD009456.

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### ET Combined With an Estrogen Agonist/Antagonist

- Tissue-selective estrogen complex (TSEC)
- Daily estrogen combined with a daily selective estrogen-receptor modulator (SERM)
- Approved for treatment of VMS and prevention of osteoporosis
- Amenorrhea rates similar to placebo
- Safety profile comparable to placebo

Archer DF, et al. *Fertil Steril*. 2009;92(3):1039-1044. Pinkerton JV, et al. *Obstet Gynecol*. 2013;121(5):959-968. Pinkerton JV, et al. *J Clin Endocrinol Metab*. 2014;99(2):E189-E198. Pickar JH, et al. *Menopause*. 2014;21(9):1033-1045.

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## Transdermal Hormone Therapy

Medications	Available doses*
Transdermal estrogen formulations for menopausal hormone therapy commonly prescribed in the United States	
Weekly estradiol patch	0.014 mg, 0.025 mg, 0.0375 mg, 0.05 mg, 0.06 mg, 0.075, 0.1 mg
	Standard: 0.0375–0.05 mg
	Low: 0.025 mg
	Ultra-low: 0.014 mg
Twice weekly estradiol patch	0.025 mg, 0.0375 mg, 0.05 mg, 0.075 mg, 0.1 mg
	Standard: 0.0375–0.05 mg
Combination transdermal estrogen progestin formulations available*	
Estrogen	Progesterin
Estradiol 0.05 mg	Norethindrone 0.14 mg, 0.25 mg
Estradiol 0.045 mg	Levonorgestrel 0.015 mg

\*Daily release note

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## Oral Hormone Therapy

Medications	Available doses
Oral estrogen formulations for menopausal hormone therapy commonly prescribed in the United States	
Estradiol	0.5 mg, 1.0 mg, 2.0 mg
	Standard: 1.0 mg
	Low: 0.5 mg
Conjugated equine estrogen	0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg
	Standard: 0.625 mg
	Low: 0.3 mg, 0.45 mg
Combination oral estrogen-progestogen formulations available	
Estradiol (0.5 mg, 1.0 mg)	Drospirenone (0.25 mg, 0.5 mg)
Estradiol (0.5 mg, 1.0 mg)	Norethindrone acetate (0.1 mg, 0.5 mg)
Estradiol (1.0 mg)	Norgestimate (0.09 mg)
Estradiol (1.0 mg)*	Progesterone (100 mg)*
Ethinyl estradiol (2.5 µg, 5 µg)	Norethindrone acetate (0.5 mg, 1.0 mg)
Conjugated equine estrogen (0.3 mg, 0.45 mg, 0.625 mg)	Medroxyprogesterone acetate (1.5 mg, 2.5 mg, 5 mg)
Oral progestogen formulations for menopausal hormone therapy commonly prescribed in the United States	
Medroxyprogesterone acetate	2.5 mg, 5 mg, 10 mg
Progesterone*	100 mg, 200 mg

\*Formulation contains peanut oil; hypnotic effect, so should be taken at bedtime.

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## Non-Hormone Prescription Therapies for VMS

- FDA-approved prescription treatments
  - Paroxetine 7.5 mg daily
  - Fezolinetant 45 mg daily
- Off-label prescription therapies
  - Selective serotonin reuptake inhibitors
  - Serotonin-norepinephrine reuptake inhibitors
  - Gabapentin
  - Oxybutynin

Carroll DG, et al. *Int J Womens Health*. 2015;7:615-624; Reddy SY, et al. *Obstet Gynecol*. 2006;108:41-48; Rada G, et al. *Cochrane Database Syst Rev*. 2010;CD004923; Simon JA, et al. *Menopause*. 2016;23(11):1214-1221.

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Non-Hormone Pharmaceuticals		
Fezolinetant	45 mg daily	Single dose, no titration needed
Selective Serotonin Reuptake Inhibitors		
Paroxetine salt	7.5 mg	Single dose, no titration needed
Paroxetine	10-25 mg/d	Start with 10 mg/d
Citalopram	10-20 mg/d	Start with 10 mg/d
Escitalopram	10-20 mg/d	Start with 10 mg/d (for sensitive or older women, start with 5 mg/d for titration, but this dose has not been evaluated for efficacy)
Serotonin Norepinephrine Reuptake Inhibitors		
Desvenlafaxine	100-150 mg/d	Start with 25-50 mg/d and titrate up by that amount each day
Venlafaxine	37.5-150 mg/d	Start with 37.5 mg/d
Gabapentin	900-2,400 mg/d	Start with 100-300 mg at night, then add 300 mg at night, then a separate dose of 300 mg in the morning (start 100 mg if concerned about sensitivity)
Oxybutynin	2.5-5 mg mg/d	Start with 2.5 mg daily and increase to 5 mg twice daily after one week

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**NON-HORMONES: RECOMMENDED**

- Cognitive-behavioral therapy (Level I)
- Clinical hypnosis (Level I)
- Fezolinetant (Level I)
- Selective serotonin reuptake inhibitors/serotonin-norepinephrine reuptake inhibitors (Level I)
- Gabapentin (Level I)
- Oxybutynin (Levels I-II)
- Weight loss (Levels II-III)
- Stellate ganglion block (Levels II-III)

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

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**NON-HORMONES: NOT RECOMMENDED**

- Paced respiration (Level I)
- Supplements/Herbal remedies (Levels I-II)
- Cooling techniques, avoiding triggers, exercise, yoga, mindfulness-based intervention, relaxation (Level II)
- Soy foods and soy extracts, soy metabolite equol (Level II)
- Cannabinoids (Level II)
- Chiropractic interventions and acupuncture (Levels I-III)
- Clonidine (Levels I-III)
- Dietary modification (Level III)
- Pregabalin (Level III)

Level I: Good and consistent scientific evidence.  
Level II: Limited or inconsistent scientific evidence.  
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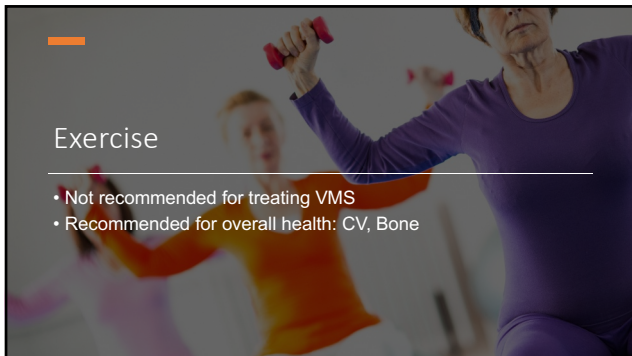
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**Exercise**

- Not recommended for treating VMS
- Recommended for overall health: CV, Bone

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**Weight loss**

Reduces VMS

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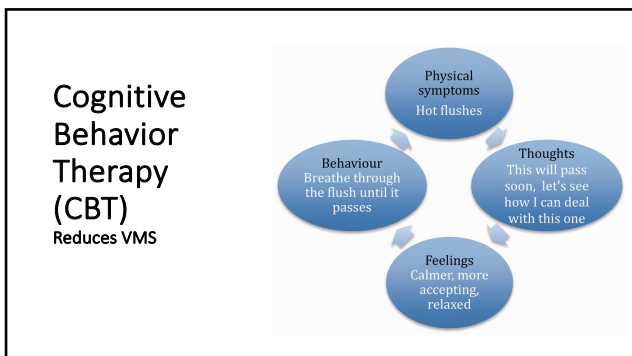
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**Cognitive Behavior Therapy (CBT)**

Reduces VMS

Physical symptoms  
Hot flushes

Thoughts  
This will pass soon, let's see how I can deal with this one

Feelings  
Calmer, more accepting, relaxed

Behaviour  
Breathe through the flush until it passes

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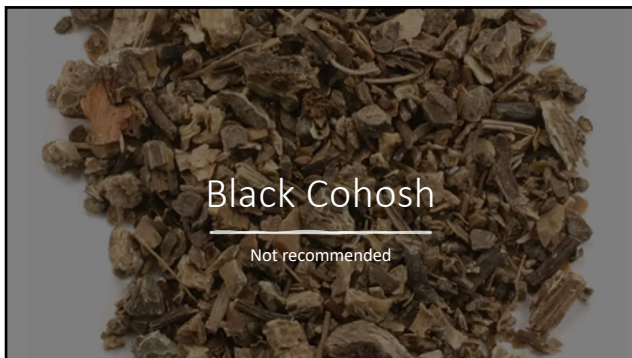
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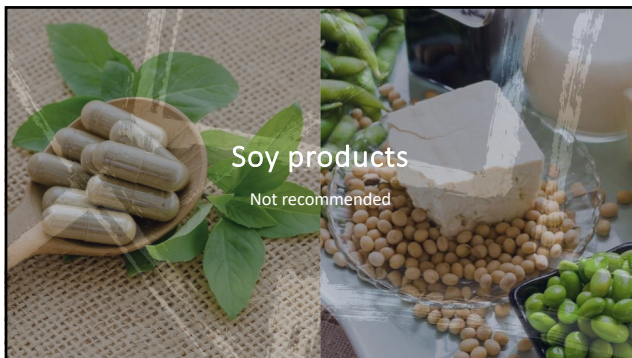
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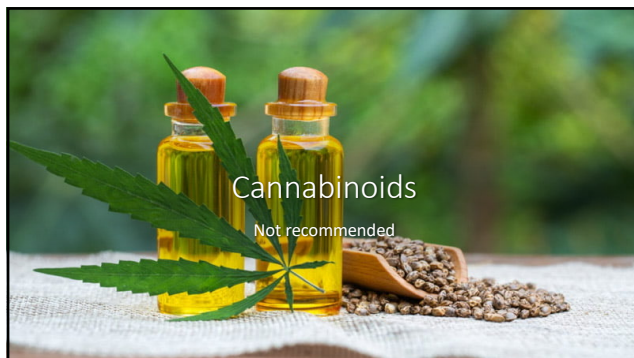
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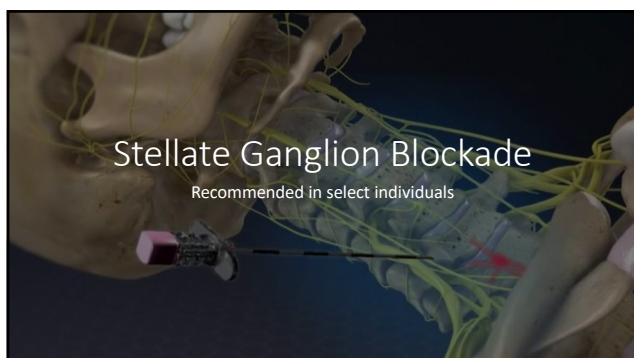
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**NON-HORMONES: NOT RECOMMENDED**

- Paced respiration (Level I)
- Supplements/Herbal remedies (Levels I-II)
- Cooling techniques, avoiding triggers, exercise, yoga, mindfulness-based intervention, relaxation (Level II)
- Soy foods and soy extracts, soy metabolite equol (Level II)
- Cannabinoids (Level II)
- Chiropractic interventions and acupuncture (Levels I-III)
- Clonidine (Levels I-III)
- Dietary modification (Level III)
- Pregabalin (Level III)

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

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### ELISE'S TREATMENT OPTIONS

- Estrogen-Progestogen Therapy (Level I)
- SSRIs/SNRIs (Level I)
- Fezolinetant (Level I)
- Gabapentin (Level I)
- Oxybutynin (Levels I-II)
- Cognitive-behavioral therapy (Level I)
- Clinical hypnosis (Level I)
- Weight loss (Levels II-III)
- Stellate ganglion block (Levels II-III)



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

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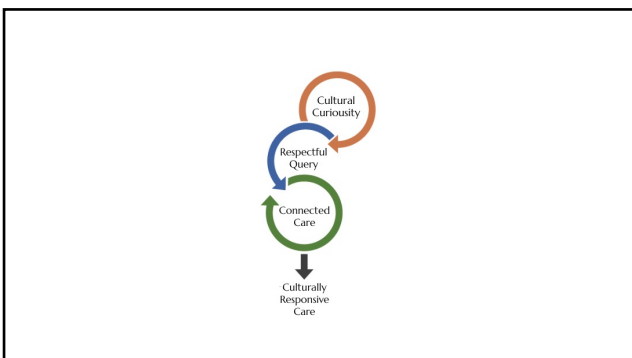
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### Cultural Curiosity

*"I am sorry you've had such a challenging time with your symptoms. Everyone's experiences menopause symptoms differently. I would like to understand more about your unique experience and your preference for natural treatment options..."*

The diagram is identical to the one on page 35, showing the flow from Cultural Curiosity to Respectful Query to Connected Care, resulting in Culturally Responsive Care.

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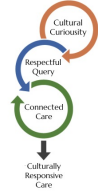
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## Respectful Query

- How and what do you feel about going through menopause?
- What advice have you received about menopause?
- Are there any cultural practices related to menopause that are important for you to observe?
- Do you have a spiritual, religious or faith practice that influences your health care?
- How do you manage your menopausal symptoms? Foods, herbs, behaviors?
- *We all want to live our best lives. Are there things that get in the way of you taking care of yourself and living your best life?*




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## Connected Care

*"Elise, I like to be sure that all of my patients receive information about all available and effective treatment options. You may not be interested in some of them, but I want to be sure that you have complete information before making a decision. Are you ok with me reviewing non-natural therapies?"*




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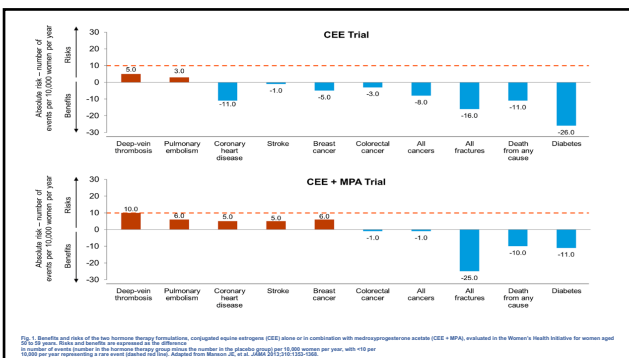
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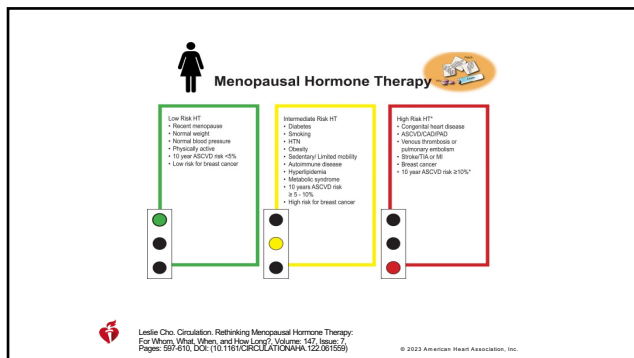
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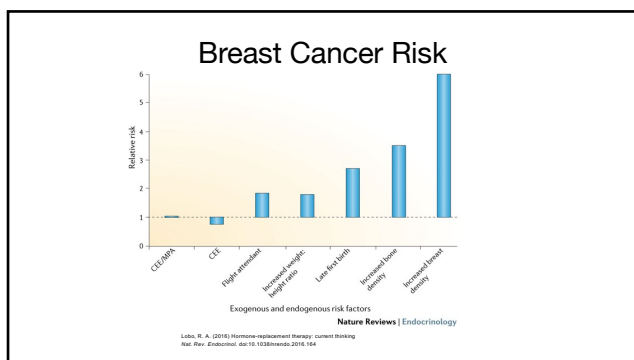
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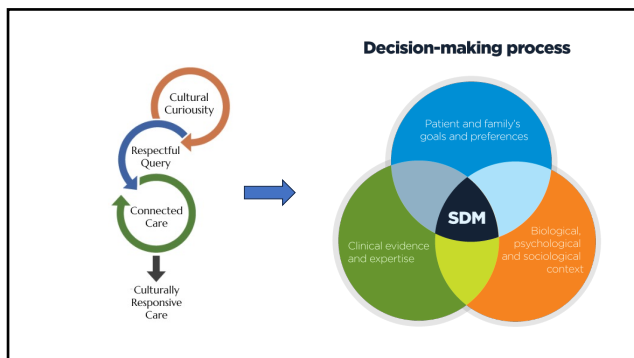
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## ELISE'S DECISION...

**Medication Treatments for Fatigue and Night Sweats**

**Medication Summary:** Medication treatments for fatigue and night sweats include antidepressants, thyroid hormone, and corticosteroids. These medications can help improve energy levels and reduce night sweats. However, they may also have side effects, such as weight gain, dry mouth, and increased risk of infection. It is important to discuss the risks and benefits of each medication with your healthcare provider.

**Recommendations:**


- Consider antidepressants, such as nortriptyline, amitriptyline, or doxepin, for fatigue and night sweats.
- Consider thyroid hormone replacement therapy if you have hypothyroidism.
- Consider corticosteroids, such as prednisone, for fatigue and night sweats.
- Consider lifestyle changes, such as regular exercise, a healthy diet, and good sleep hygiene, to help improve energy levels and reduce night sweats.
- Consider complementary and alternative medicine, such as acupuncture, yoga, and meditation, to help improve energy levels and reduce night sweats.

**Dealing With Hormone Therapy Risks**

**Dealing With Hormone Therapy Risks:** Hormone therapy can help relieve symptoms of menopause, but it also carries risks. These risks include an increased risk of heart disease, stroke, and blood clots. It is important to discuss the risks and benefits of hormone therapy with your healthcare provider. There are also non-hormonal options available for managing menopause symptoms.

**Recommendations:**

- Consider non-hormonal options, such as antidepressants, for managing menopause symptoms.
- Consider lifestyle changes, such as regular exercise, a healthy diet, and good sleep hygiene, to help manage menopause symptoms.
- Consider complementary and alternative medicine, such as acupuncture, yoga, and meditation, to help manage menopause symptoms.



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