

# 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.*

A photograph of two women embracing. The woman on the left is older, wearing a light-colored patterned headscarf and a white t-shirt. The woman on the right is younger, with dark curly hair, wearing a grey top. They are both smiling gently at the camera. The background is a blurred outdoor setting with a building and trees.

# Can we talk?

## Genitourinary Symptoms of Menopause in Cancer Survivors

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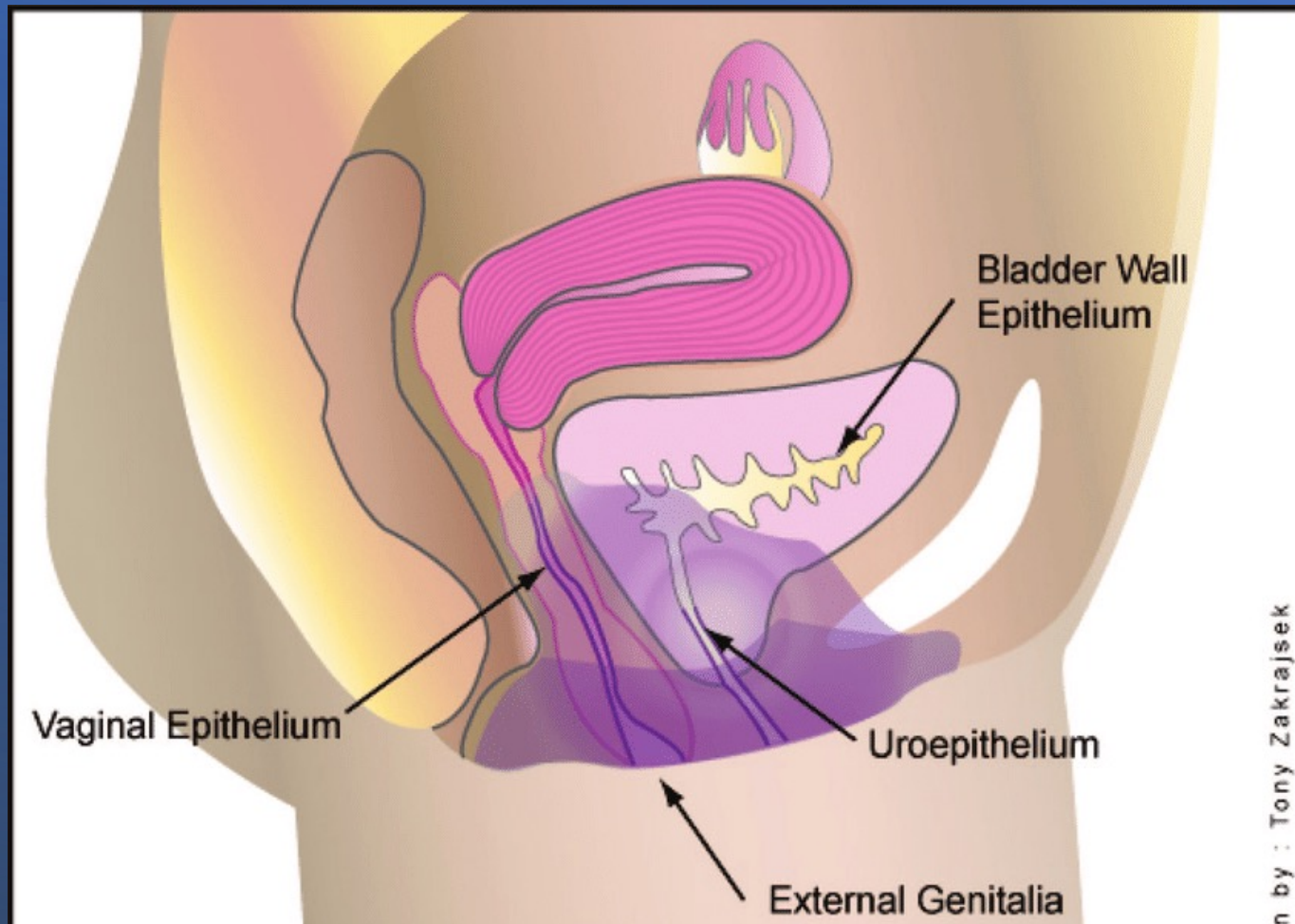
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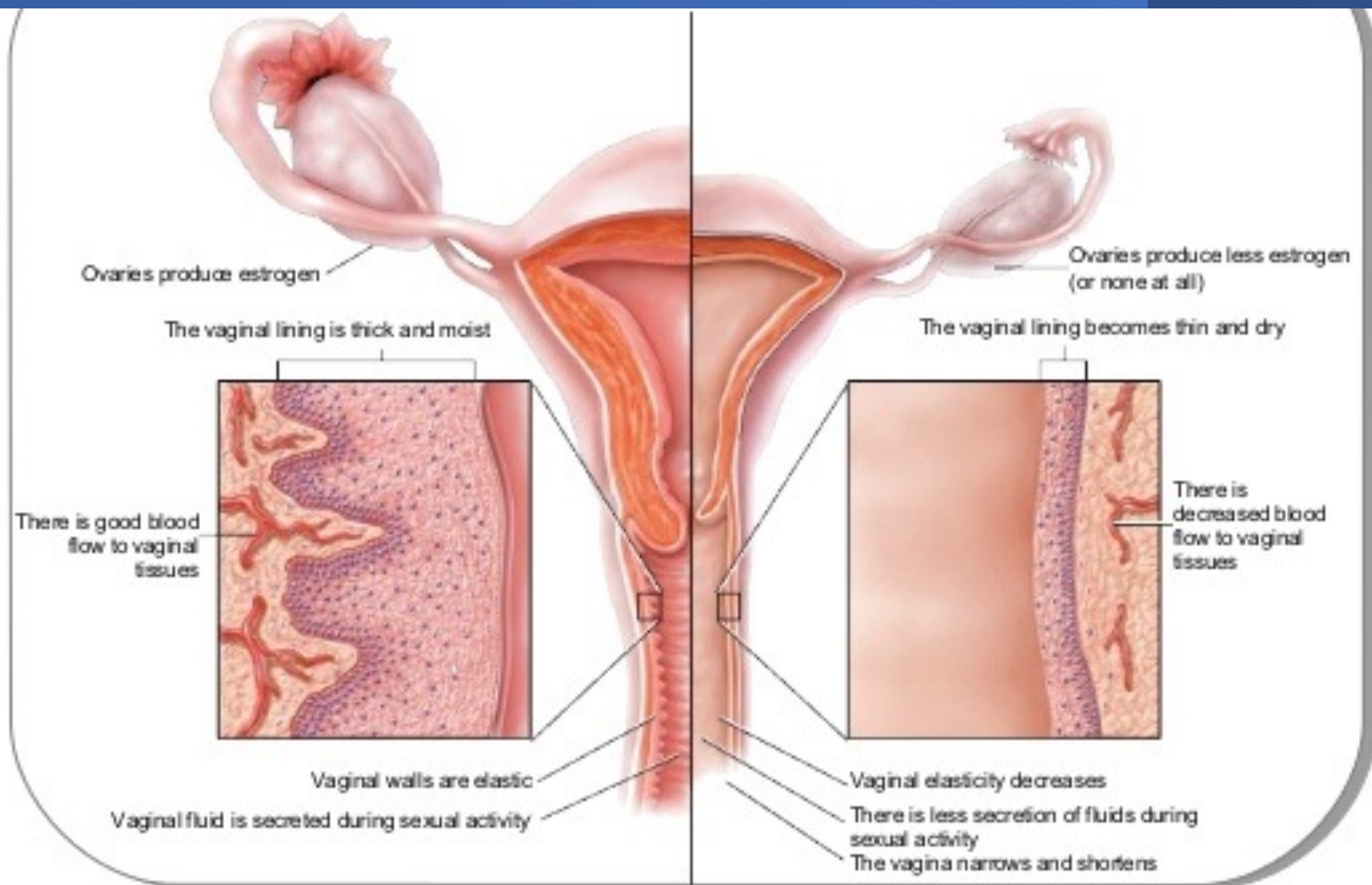
# Objectives

- Discuss symptom presentation of the genitourinary syndrome of menopause in cancer survivors
- Review consensus recommendations for treating the genitourinary syndrome of menopause in cancer survivors



| System           | Tissues                                     | Expressed Estrogen Receptors (ER) |
|------------------|---|-----------------------------------|
| Reproductive     | Uterus, Vagina                              | ER $\alpha$ , ER $\beta$ , GPER   |
| Urinary          | Bladder, Urethra                            | ER $\beta$                        |
| Gastrointestinal | Bowel, External Anal Sphincter              | ER $\alpha$ , ER $\beta$          |
| Musculoskeletal  | Pelvic Floor Muscles, Uterosacral Ligaments | ER $\alpha$ , ER $\beta$          |







Surgery: Oophorectomy,  
Vulvectomy, Hysterectomy



Chemotherapy: ovarian toxicity and dysfunction,  
neuropathy



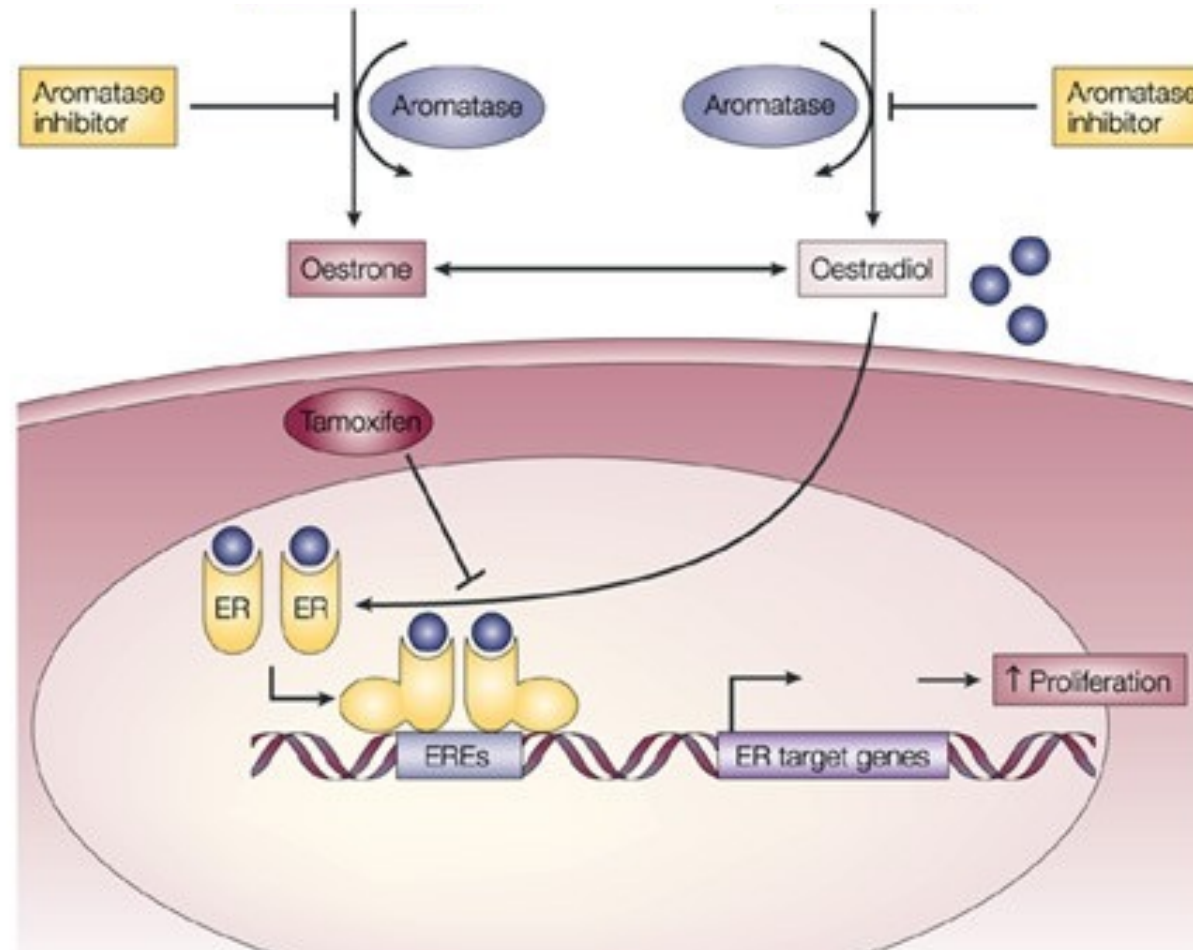


**Pelvic Radiation:** direct tissue damage, radiation vaginitis, vaginal fibrosis, mucositis, shortening, stenosis





Tamoxifen: estrogenic effect, increased vaginal secretions

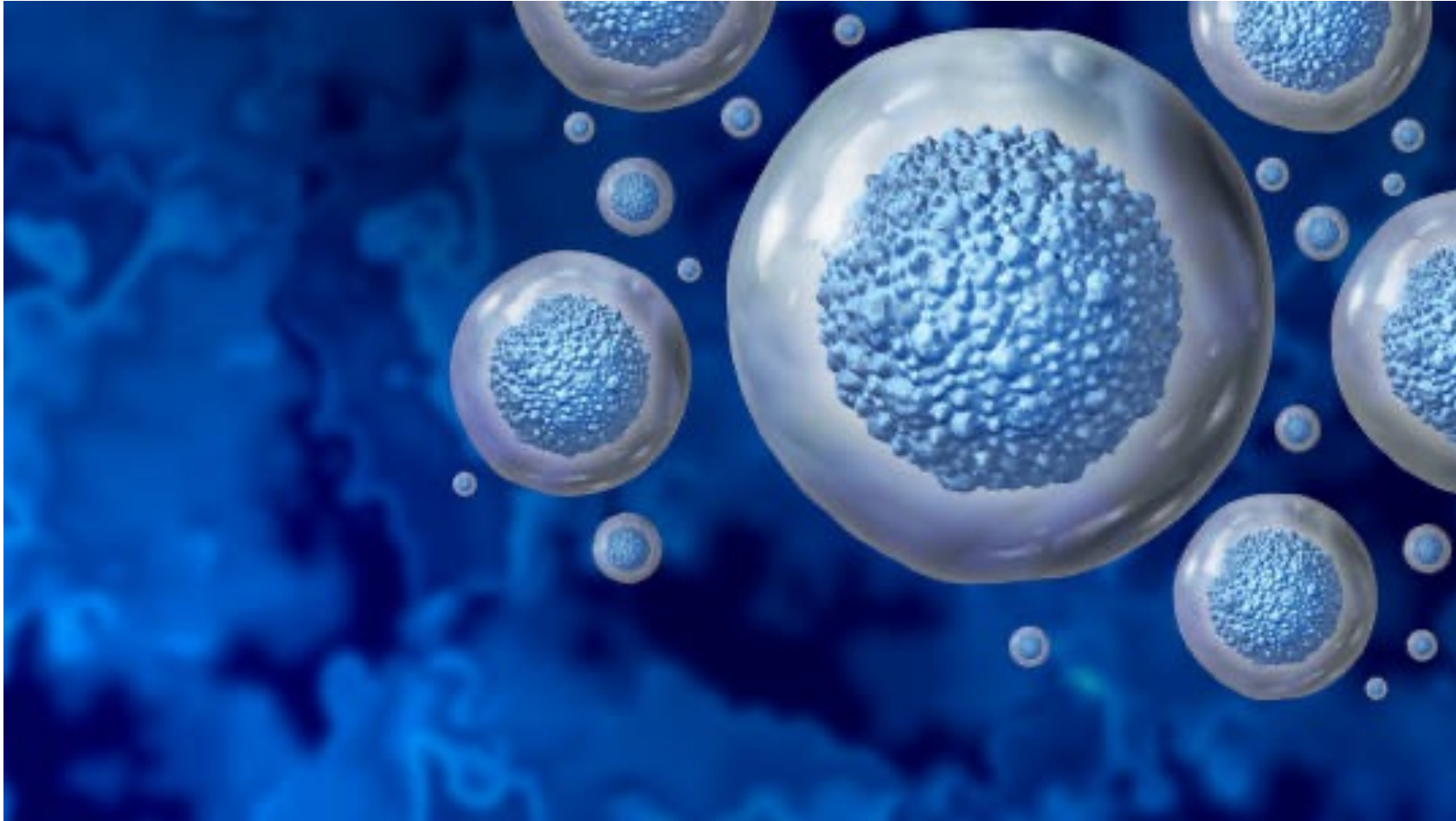


**Aromatase Inhibitors :**  
 marked vaginal dryness, vulvar thinning, sexual discomfort

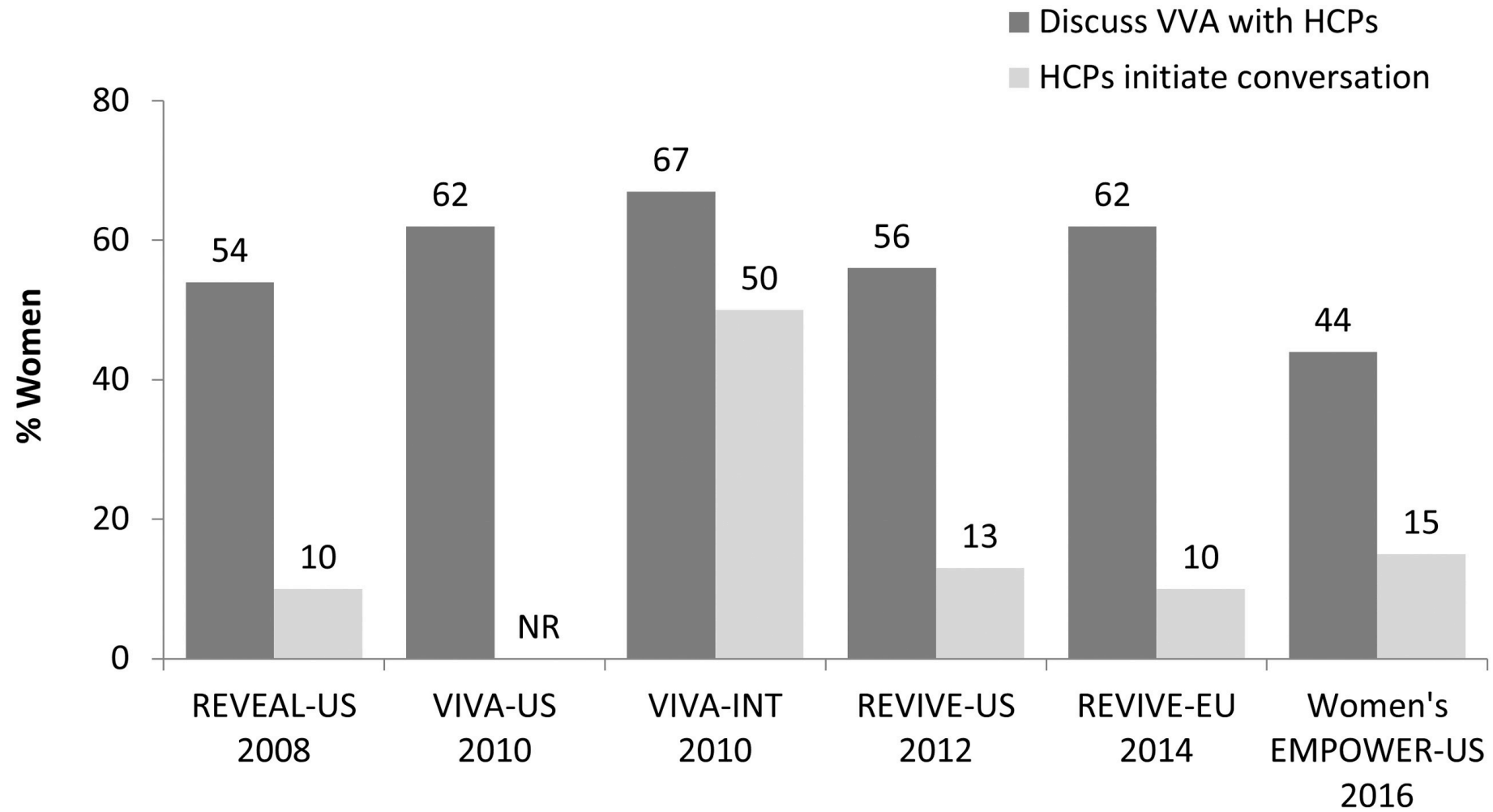


Immunotherapy: inflammation, GSM pain exacerbation





Stem Cell Transplant: GVHD: vulvovaginal dryness, pain, dyspareunia







## Symptoms

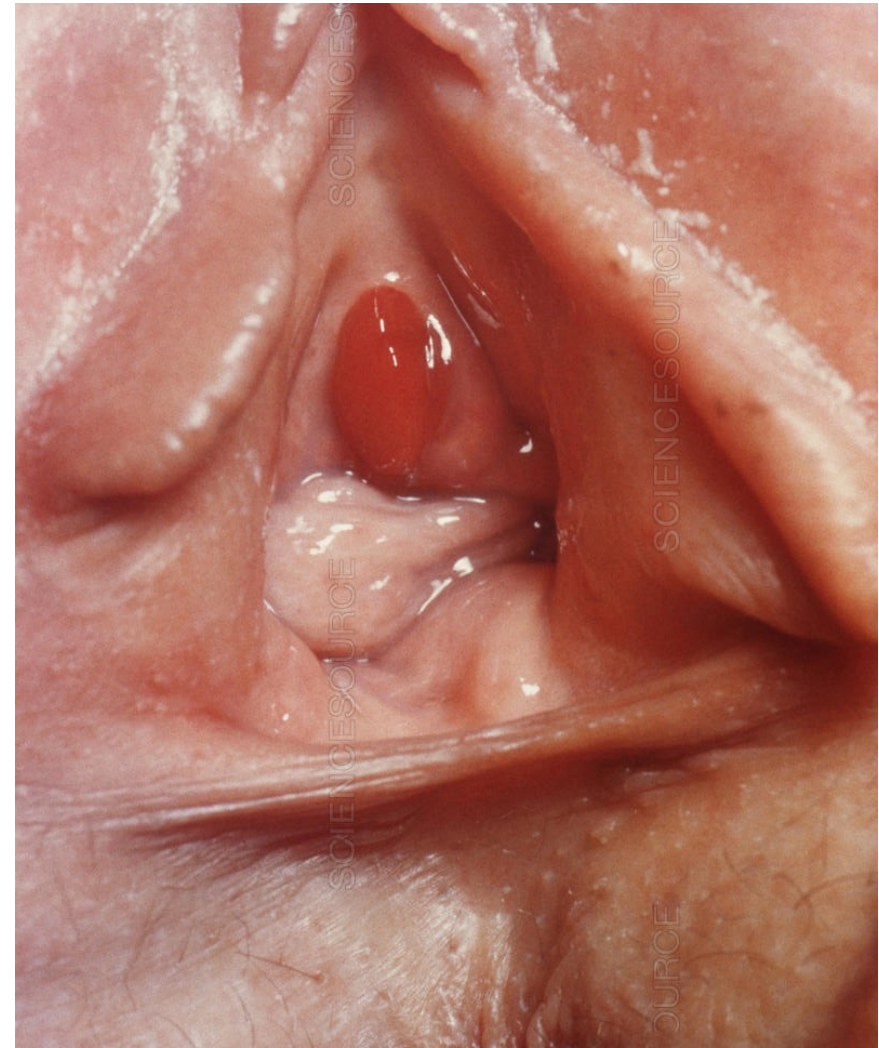
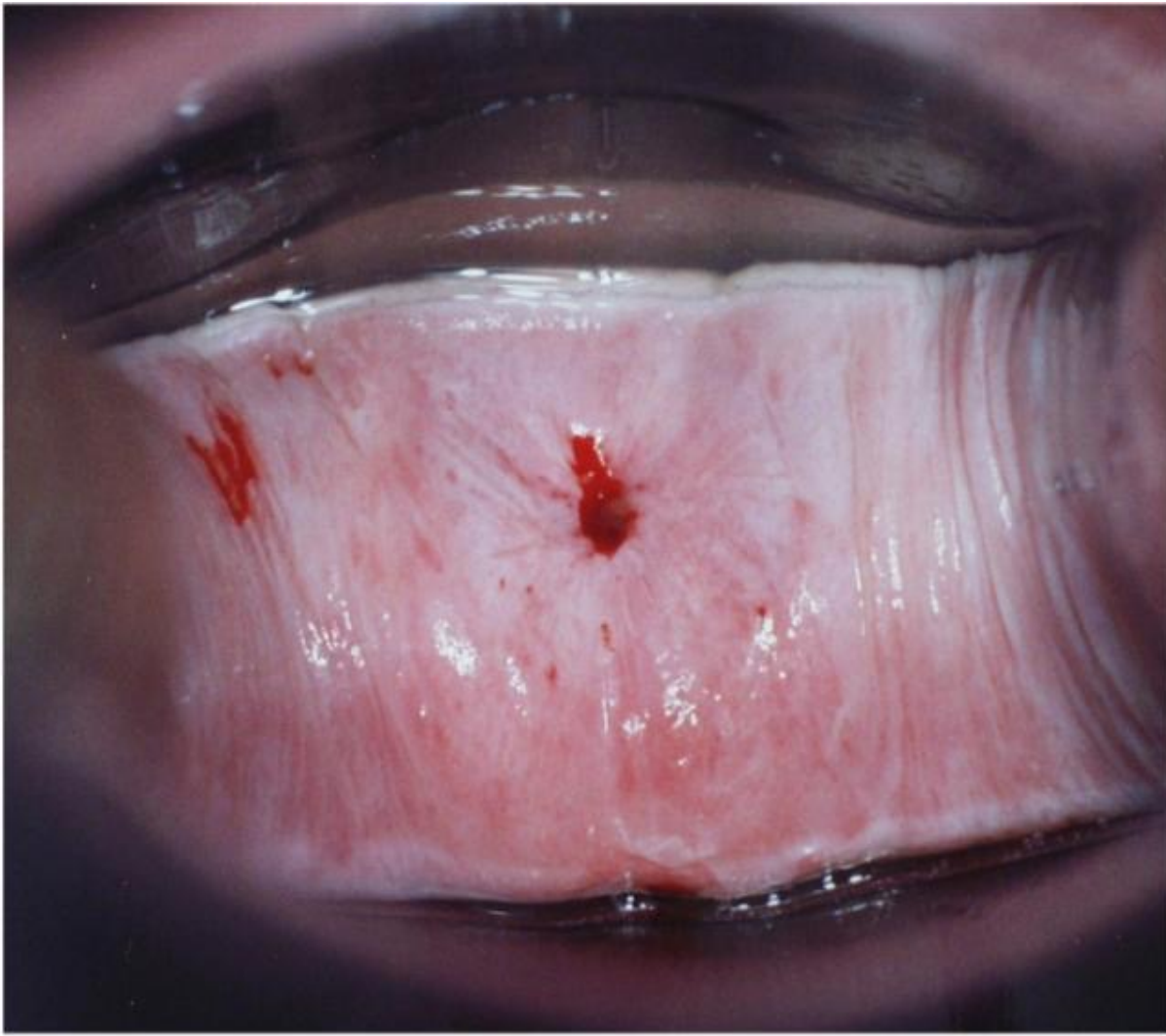
- Genital dryness
- Decreased lubrication with sexual activity
- Discomfort or pain with sexual activity
- Post-coital bleeding
- Decreased arousal, orgasm, desire
- Irritation/Burning/Itching of vulva or vagina
- Dysuria
- Urinary frequency/urgency



## Signs

- Decreased moisture
- Decreased elasticity
- Labia minora resorption
- Pallor/Erythema
- Loss of vaginal rugae
- Tissue fragility/fissures/petechiae
- Urethral eversion or prolapse
- Loss of hymenal remnants
- Prominence of urethral meatus
- Introital retraction
- Recurrent urinary tract infections

# Genitourinary Syndrome of Menopause



GSM in Cancer Survivors

- Complete medical history
    - Symptom characterization, prior treatments
    - Review of vaginal irritants
  - Sexual history
  - Physical examination
    - Vaginal pH and wet prep as indicated
    - Vulvar/Vaginal cultures as appropriate
    - Biopsy white, pigmented, or thickened lesions
- Any vulvar lesion that does not respond to treatment should be biopsied

## GSM: History and Evaluation



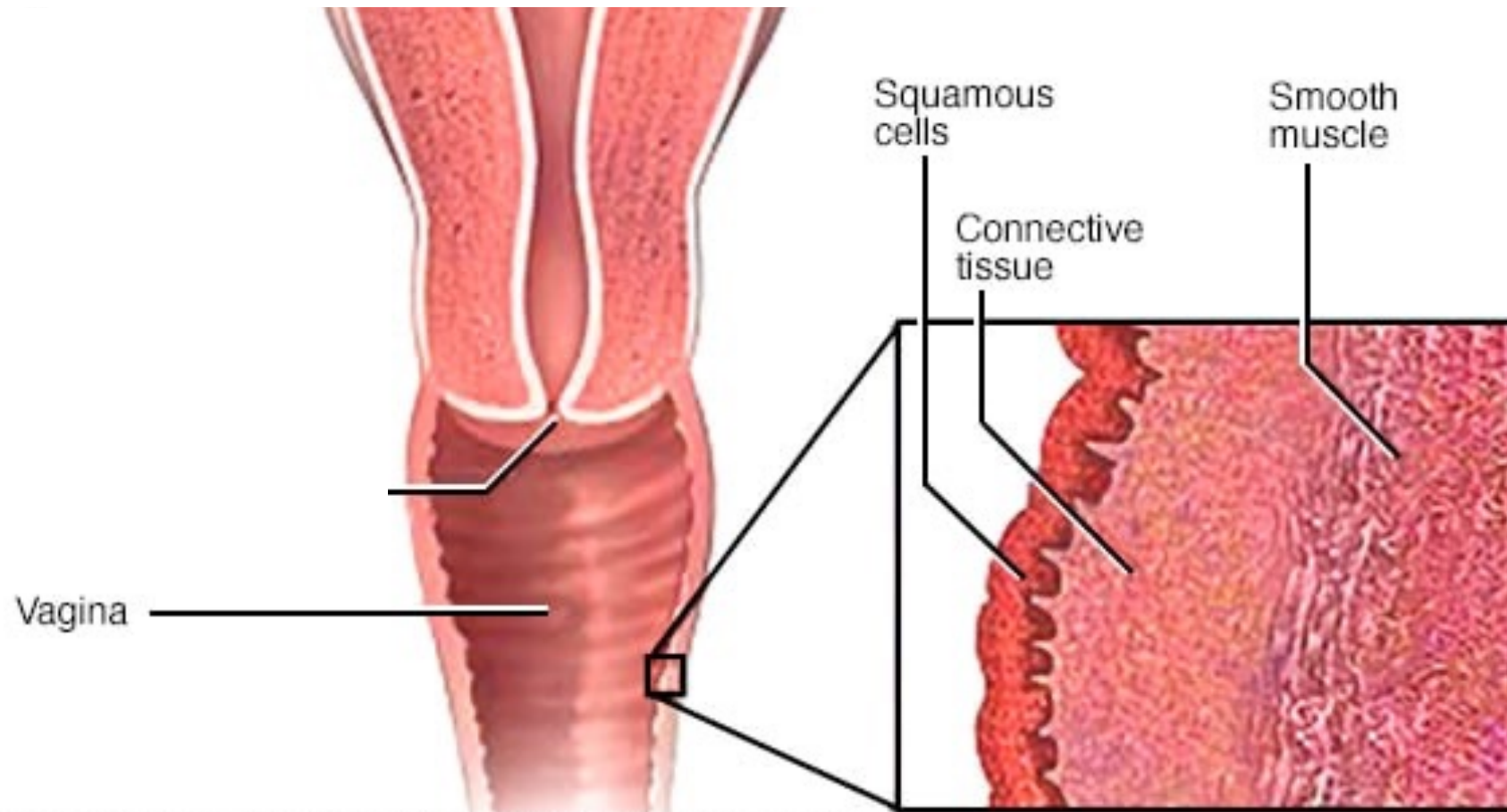
- 41% of oncologists refer patients with GSM to gynecologists
- Only 35% of oncologists manage symptoms independently
- Shared Decision making

GSM: Treatment



The

3Rs



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# Layers of Vaginal Tissue



# Treatments for GSM: Lubricants

- Reduce friction
- Short term comfort
- One size does not fit all-encourage patients to try different formulations: water based vs. silicone
- Consider osmolality and pH
  - Ideal osmolality: of  $< 380$  mOsm/kg,
  - Ideal pH  $> 3.0$
- Avoid additives irritating additives: parabens, glycerin, flavors, spermicides

# Treatments for GSM: Moisturizers

- Retain moisture
- One size does not fit all-encourage patients to try different formulations
- More frequent use compared to naturally menopausal women:
  - Consider daily use
  - Titrate to patient preference/tolerance

# Treatments for GSM: Lubricants and Moisturizers

| Lubricants   |   | Moisturizers   |
|--|---|--|
| <i>Water based</i><br>Astroglide Liquid<br>Astroglide Gel Liquid<br>Astroglide<br>Good Clean Love<br>Just Like Me<br>K-Y Jelly<br>Pre-Seed<br>Slippery Stuff<br>Liquid Silk<br>YES WB<br>SYLK<br>Sliquid | <i>Silicone based</i><br>Astroglide X<br>ID Millennium<br>K-Y Intrigue<br>Pink<br>Pjur Eros<br>Uberlube<br>Sliquid<br><br><i>Oil based</i><br>Élégance Women's<br>Lubricants<br>Olive oil<br>YES OB | Replens<br>Me Again<br>Feminase<br>K-Y SILK-Eluvena<br>Revaree<br>Silken Secret<br>Hyalo-gyn |

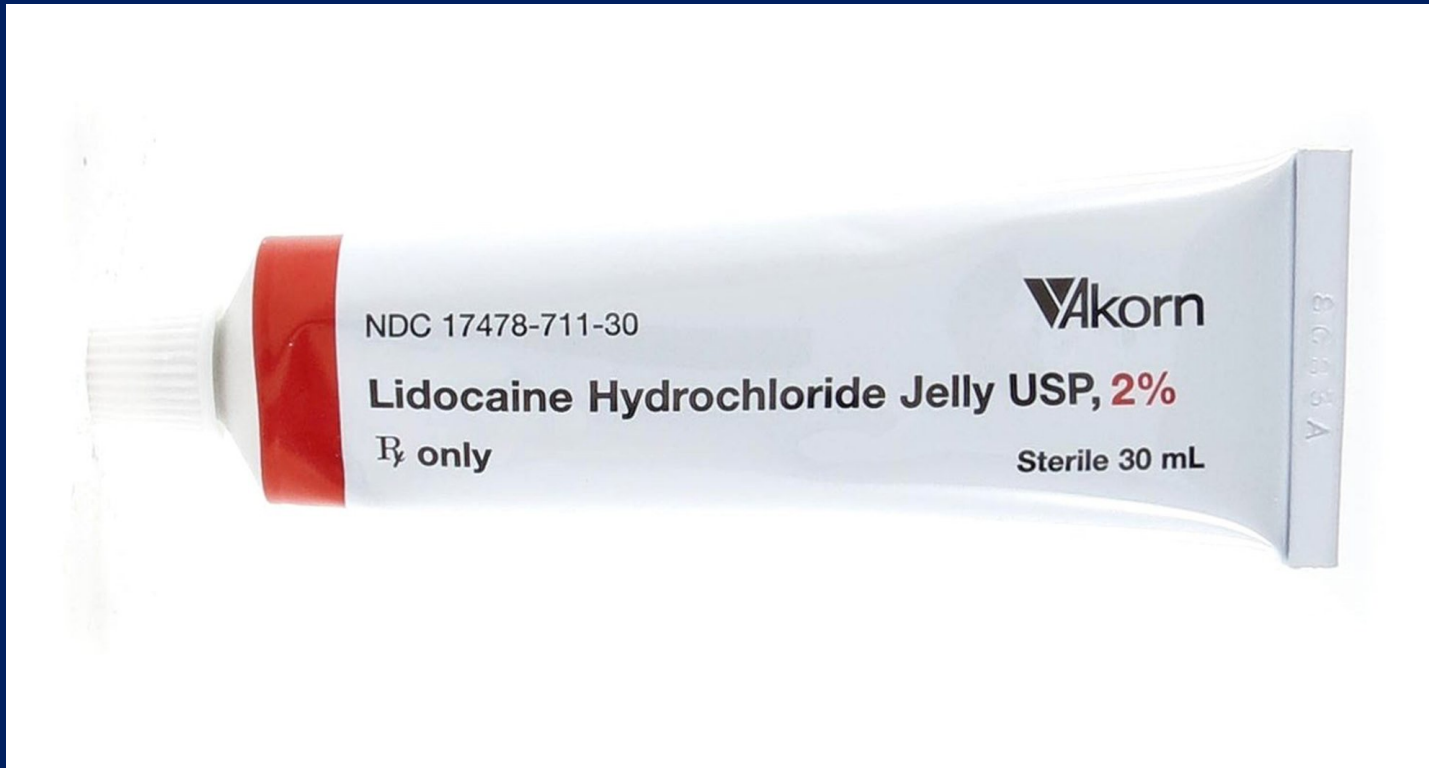


# Treatments for GSM: Kitchen cabinet?

- Natural oils: olive, coconut may be associated with vaginal infections
- Probiotics: could be helpful to microbiome, need comprehensive trials

# Treatments for GSM: Lidocaine

- Apply with cotton swab ~3 minutes before penetration

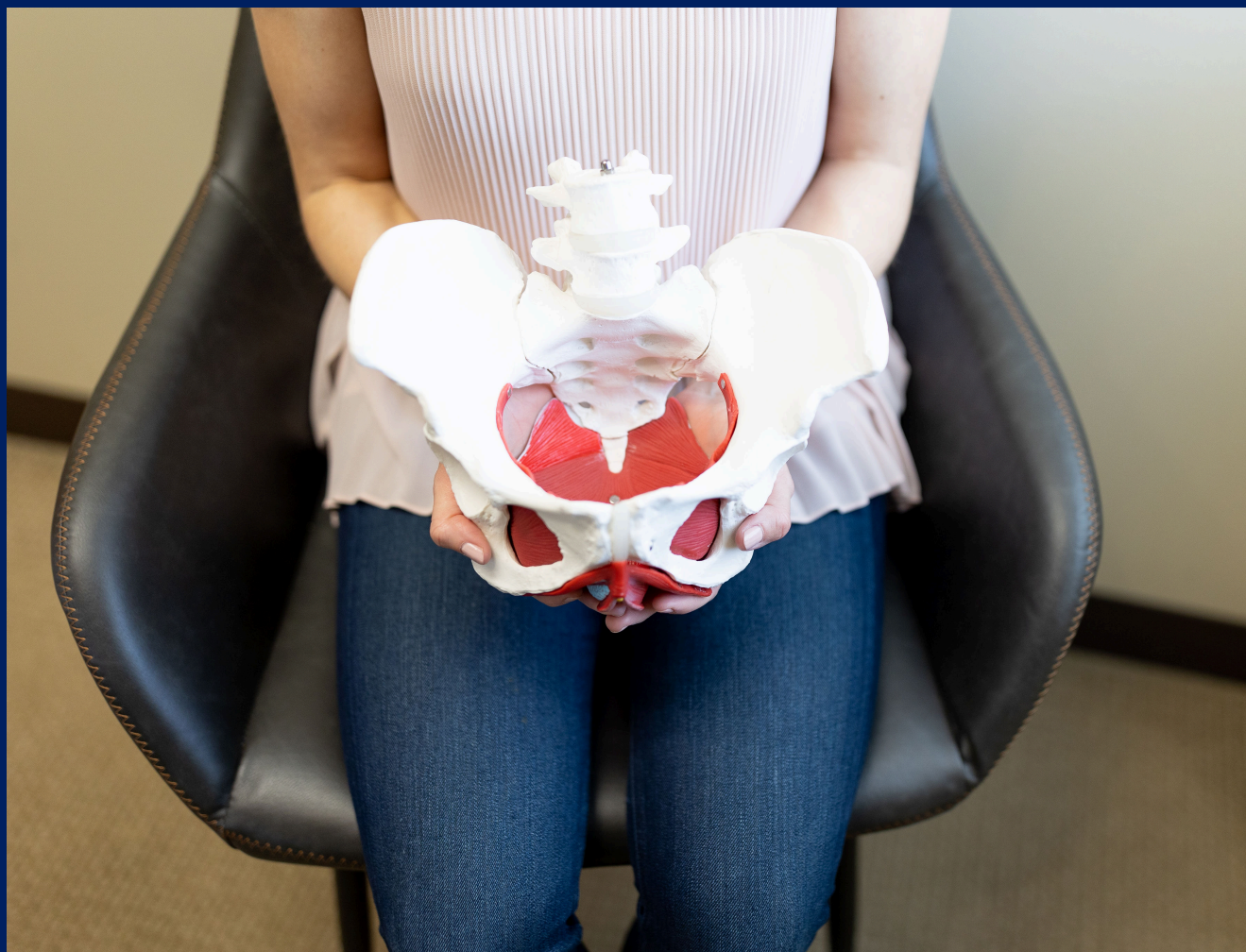


# Treatments for GSM: Vaginal Dilators





# Treatments for GSM: PFPT



# Treatments for GSM: Psychosocial Support

- Counseling
- Psychotherapy: CBT
- Support groups
- Group and individual education

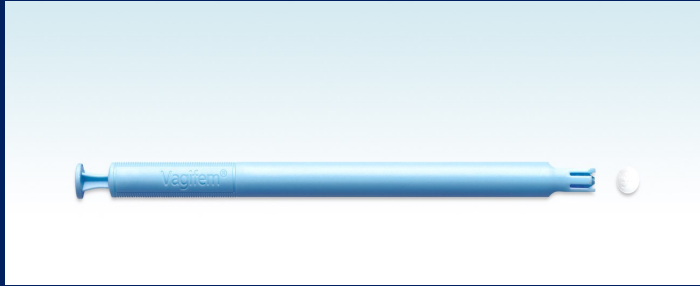




# Treatment Options



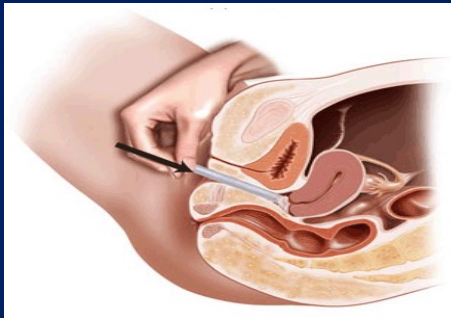
# GSM Treatment Options: Vaginal Estrogen



10 mcg Estradiol hemihydrate vaginal tablet



17 $\beta$  Estradiol Vaginal ring



Estradiol or Conjugated Equine Estrogen Cream



4 or 10 mcg Estradiol vaginal insert

# Hormone Treatments: Low-dose Vaginal Estrogen

- Restores vaginal blood flow
- Decreases vaginal pH
- Improves thickness and elasticity of vulvovaginal tissues
- Many different formulations: vaginal ring, tablets, inserts, creams
- Improvements within a few weeks, full efficacy in 2-3 mo
- Serum levels typically in postmenopause range
- Large observational studies show no increased risk of endometrial cancer, breast cancer, or CVD
- Progestogen generally is not indicated
- Controversial data/guidance in hormone sensitive cancer survivors: Shared Decision-Making

# Local Estrogen Therapy

## Women at high risk for breast cancer

- failed nonhormonal treatment

## Women with ER positive breast cancers on tamoxifen

- persistent, severe symptoms with failed nonhormonal treatments and factors suggesting a low risk of recurrence

## Women with ER positive breast cancers on AI

- persistent, severe symptoms with failed nonhormonal treatments and factors suggesting a low risk of recurrence
- consult with the oncologist to consider switching to tamoxifen

## Women with triple negative breast cancers

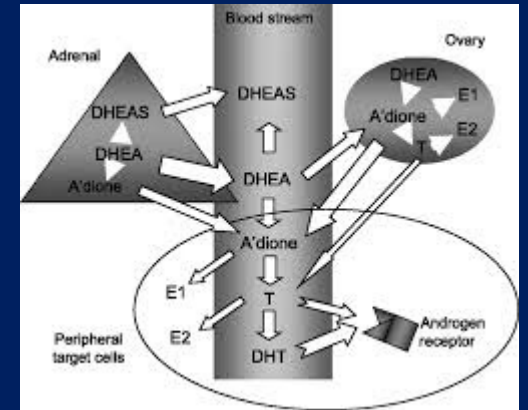
- Theoretically reasonable data are lacking

## Women with metastatic disease

- QoL, comfort, and intimacy may be a priority for many women with metastatic disease

# Hormone Treatments: Dehydroepiandrosterone (DHEA)

- 0.5%/6.5 mg DHEA vaginal suppository: Prasterone
- Indication: FDA approved for moderate to severe dyspareunia secondary to VVA
- Directions: inserted once daily at bedtime
- Phase 3 RCT showed significantly improved
  - Vaginal maturation index (VMI)
  - Vaginal pH
  - Signs of atrophy
  - Vaginal dryness
  - Dyspareunia
- Serum steroid levels remained within the normal postmenopause range
- Only adverse event (AE): vaginal discharge because of melting of the vehicle
- Safety: endometrial safety confirmed at 1 y





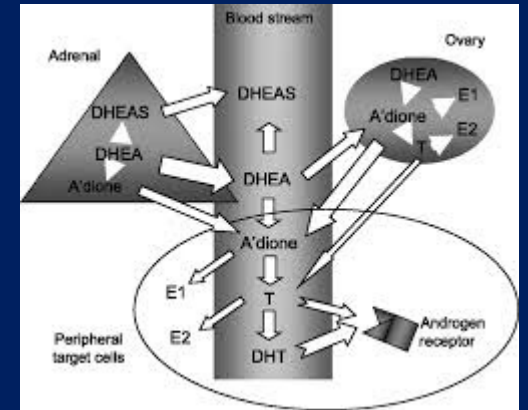
# Hormone Treatments: Ospemifene

- **Oral** SERM: estrogen agonist/antagonist
- Indication: FDA approved for moderate to severe dyspareunia associated with VVA
- Dose: 60 mg/day
- Improves
  - VMI
  - Vaginal pH
  - Symptoms of VVA
  - May take 6 months to achieve full efficacy
- Safety
  - No endometrial hyperplasia or cancer (at 52 w)
  - Can increase VMS
  - May increase the risk of venous thromboembolism (VTE)
- Antiestrogenic effects on breast but not approved for women with breast cancer
- **NOT RECOMMENDED IN BREAST CANCER PATIES**



# Hormone Treatments: Dehydroepiandrosterone (DHEA)

- 6.5 mg DHEA vaginal suppository: Prasterone
- Indication: FDA approved for moderate to severe dyspareunia secondary to VVA
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  - Vaginal dryness
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- Serum steroid levels remained within the normal postmenopause range
- Only adverse event (AE): vaginal discharge because of melting of the vehicle
- Safety: endometrial safety confirmed at 1 y
- **CAN BE CONSIDERED IN BREAST CANCER PATIENTS**



# Hormone Treatments: Ospemifene

- **Oral** SERM: estrogen agonist/antagonist
- Indication: FDA approved for moderate to severe dyspareunia associated with VVA
- Directions: daily oral administration (60 mg)
- Improves
  - VMI
  - Vaginal pH
  - Symptoms of VVA
  - May take 6 months to achieve full efficacy
- Safety
  - No endometrial hyperplasia or cancer (at 52 w)
  - Can increase VMS
  - May increase the risk of venous thromboembolism (VTE)
- Antiestrogenic effects on breast but not approved for women with breast cancer
- Favorable effects on bone



# Treatments for GSM: Laser



Laser therapy may be considered in women who prefer a nonhormonal approach; women must be counseled regarding lack of long-term safety and efficacy data



# Take Aways

- Load the Boat: Multidisciplinary Team Approach
- Reduce friction: Lubricants
- Retain moisture: Moisturizers
- Restore vaginal and urogenital tissues: Estrogen therapy
- Reduce pain: Lidocaine
- Maintain patency and caliber: Dilators
- Low threshold for PFPT
- Individualization and Shared Decision Making for all patients, especially those with hormone sensitive cancers using Ais:
  - Consult oncologic team
  - Evaluate patient preference, goals and concerns
  - Shared decision making with patient
  - Mitigate risk

# Local Estrogen Therapy

## Women at high risk for breast cancer

- failed nonhormonal treatment

## Women with ER positive breast cancers on tamoxifen

- persistent, severe symptoms with failed nonhormonal treatments and factors suggesting a low risk of recurrence
- Observational data do not suggest increased risk of breast cancer with systemic or local estrogen therapies beyond baseline risk

## Women with ER positive breast cancers on AI

- persistent, severe symptoms with failed nonhormonal treatments and factors suggesting a low risk of recurrence
- consult with the oncologist to consider switching to tamoxifen

## Women with triple negative breast cancers

- Theoretically reasonable data are lacking

## Women with metastatic disease

QoL, comfort, and intimacy may be a priority for many women with metastatic disease

Questions?

