AOIFE O'SULLIVAN, MD MSCP

GENITOURINARY SYNDROME OF MENPAUSE

OAFP Lunch and Learn
10/15/24

DISCLOSURES

- Nothing to disclose

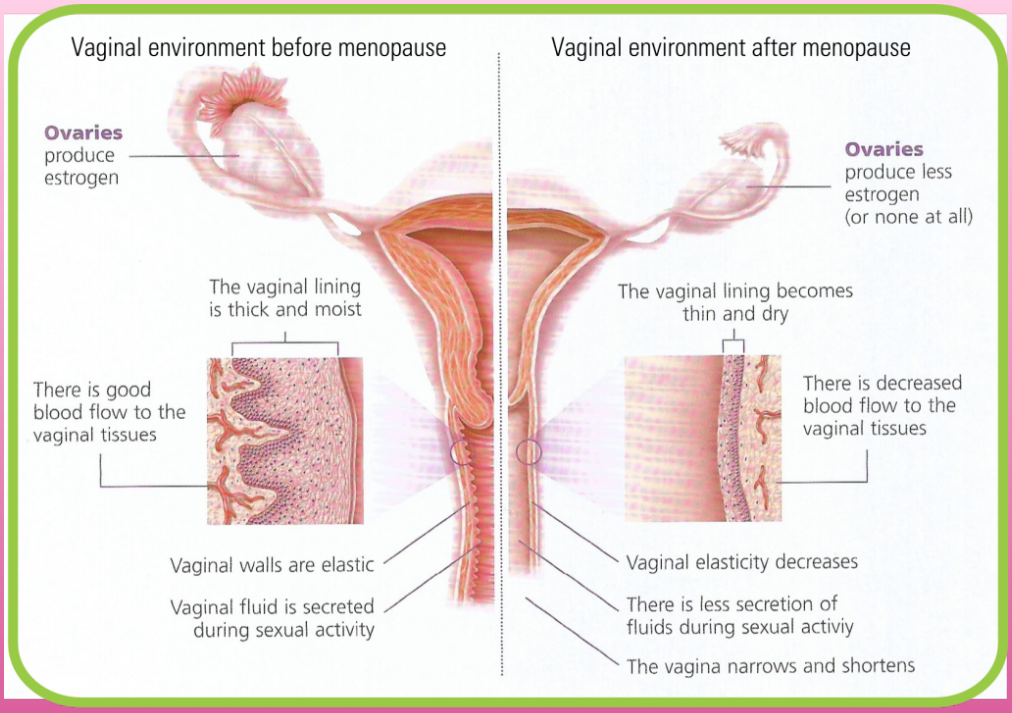
ABOUT ME

- Medical School in Ireland 1995-2001
- Family Medicine Residency in Ireland 2001-2004
- Family Medicine Residency at The University of Maryland 2004-2007
- Out-patient medicine, ER, Urgent Care, Gender-Affirming Care, Menopause Care
- Now I practice mainly midlife women's care
- I teach clinicians and the public
- Menopause Society Certified Practitioner (MSCP)
- Member of the International Menopause Society (IMS)
- Member of the International Society for the study of Women's Sexual Health (ISSWSH)
- First hand perimenopausal experience!

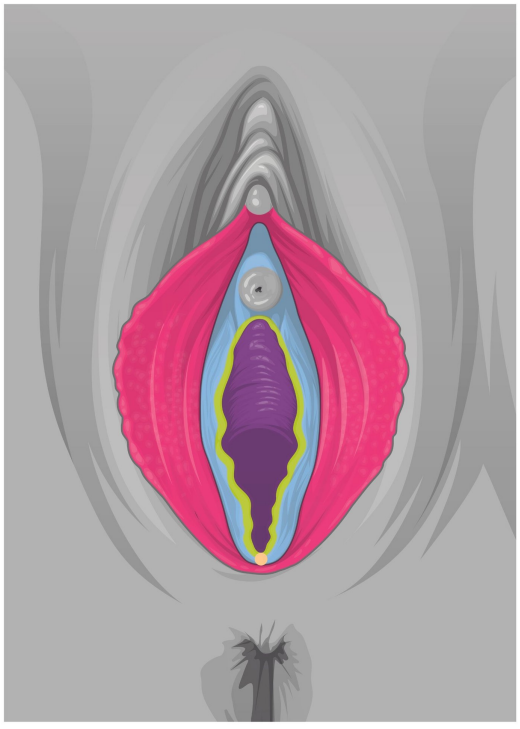
LEARNING OBJECTIVES

- Identify the GU changes experienced during periods of low hormones
- Learn how to treat them
- Dispel myths about the dangers of local vulvo-vaginal hormone treatment

- Please put your questions in the chat as we go along and we can go through each of them after the slides



Reference :
Johnston L. The Recognition and Management of Atrophic Vaginitis. *Geriatrics & Aging* 2002; 5(7):9-15.



Inner labia

Vestibule

Hymen

Vaginal canal

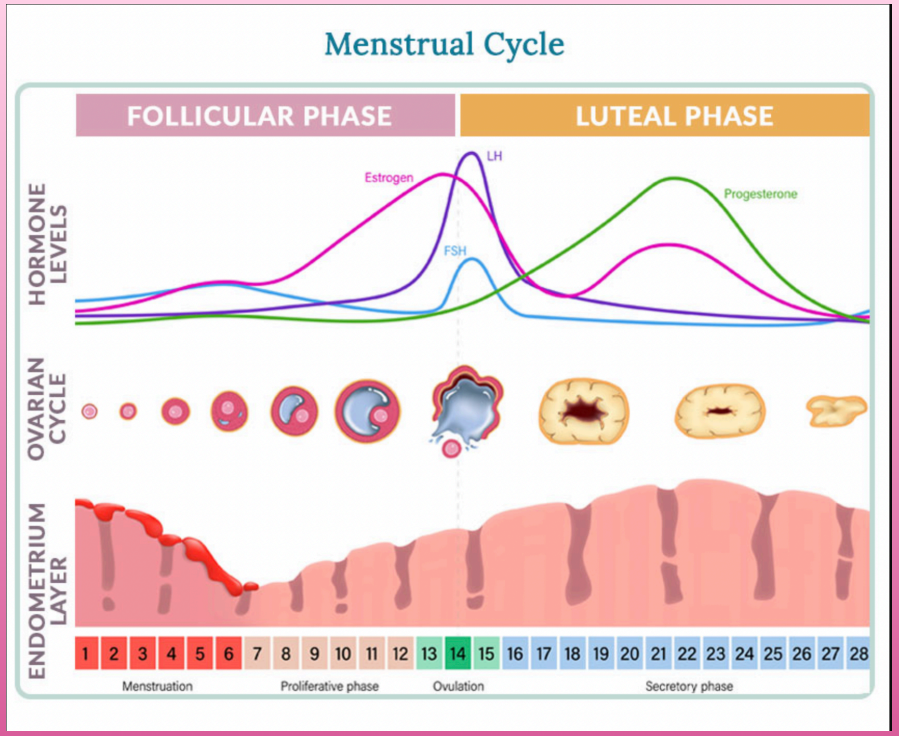
Posterior fourchette
(part of vestibule)

PELVIC GLOBAL
www.pelvicglobal.com

GENITOURINARY SYNDROME OF MENOPAUSE

- A term to describe the signs & symptoms associated with estrogen and often testosterone deficiency in the pelvis
- Changes in bladder, urethra, vagina, vulvar vestibule
- Chronic and progressive
- Women will not bring it up voluntarily, we must ask and examine
- Systemic MHT does not control GSM in around 40% of women
- With normal levels of hormones in the vagina & vulva the epithelial cells produce glycogen, the microbiome uses the glycogen as food. With low levels of hormones - no glycogen, natural microbiome dies, pH increases, we are also losing collagen & elastin and that great blood supply - we sustain massive changes & loss of function in those tissues

Portman DJ, et al. *Menopause*. 2014;21(10):1063-1068; Mac Bride MB, et al . *Mayo Clin Proc.* 2010;85(1):87-94; The NAMS 2020 Genitourinary Syndrome of Menopause Position Statement Editorial Panel. *Menopause.* 2020;27(9):976-992.



https://www.womenshealthnetwork.com/pms-and-menstruation/your-menstrual-cycle-the-basics/

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

https://www.menopause.org/docs/default-source/default-document-library/2020-gsm-ps.pdf

GSM SYMPTOMS

- Due to decreased collagen & elastin production & decreased blood supply, causes a loss of tissue 'thickness' and LOSS OF FUNCTION
- Genital dryness, decreased lubrication
- Dyspareunia, post-coital bleeding
- Decreased desire, arousal and orgasm
- Irritation, burning, itching of vulva and vagina
- Dysuria
- Urinary frequency and nocturia
- Urinary urgency
- Recurrent UTIs

Portman DJ, Gass ML; Vulvovaginal Atrophy Terminology Consensus Conference Panel. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. Maturitas. 2014 Nov;79(3):349-54. doi: 10.1016/j.maturitas.2014.07.013. Epub 2014 Aug 19. PMID: 25179577.

GSM SIGNS

- Decreased moisture and elasticity
- Resorption of labia minor
- Pallor, erythema
- Loss of vaginal rugae
- Tissue fragility, fissures, petechiae
- Prominence of urethral meatus, urethral eversion and prolapse
- Introital narrowing and retraction
- Recurrent UTIs

Portman DJ, Gass ML; Vulvovaginal Atrophy Terminology Consensus Conference Panel. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. Maturitas. 2014 Nov;79(3):349-54. doi: 10.1016/j.maturitas.2014.07.013. Epub 2014 Aug 19. PMID: 25179577.

Approved by the AUA Board of Directors April 2019

Authors' disclosure of potential conflicts of interest and author/staff contributions appear at the end of the article.

American Urological Association (AUA)/Canadian Urological Association (CUA)/
Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU)

Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline

Estrogen

16. In peri- and post-menopausal women with rUTIs, clinicians should recommend vaginal estrogen therapy to reduce the risk of future UTIs if there is no contraindication to estrogen therapy. (Moderate Recommendation; Evidence Level: Grade B)

› Urol Pract. 2024 Mar;11(2):257-266. doi: 10.1097/UPJ.0000000000000513. Epub 2023 Dec 28.

A Cost Savings Analysis of Topical Estrogen Therapy in Urinary Tract Infection Prevention Among Postmenopausal Women

Charlotte Goldman Houston [1], William S Azar [1], Sean Shenghsiu Huang [2], Rachel Rubin [1], C Scott Dorris [3], Rachael D Sussman [1]

Affiliations + expand

PMID: 38154005 DOI: 10.1097/UPJ.0000000000000513

Abstract

Introduction: UTIs are some of the most common infections in geriatric patients, with many women experiencing recurrent infections after menopause. In the US, annual UTI-related costs are $2 billion, with recurrent infections creating a significant economic burden. Given the data published on topical estrogen in reducing the number of infections for postmenopausal women with recurrent UTI, we sought to evaluate how this would translate to cost savings.

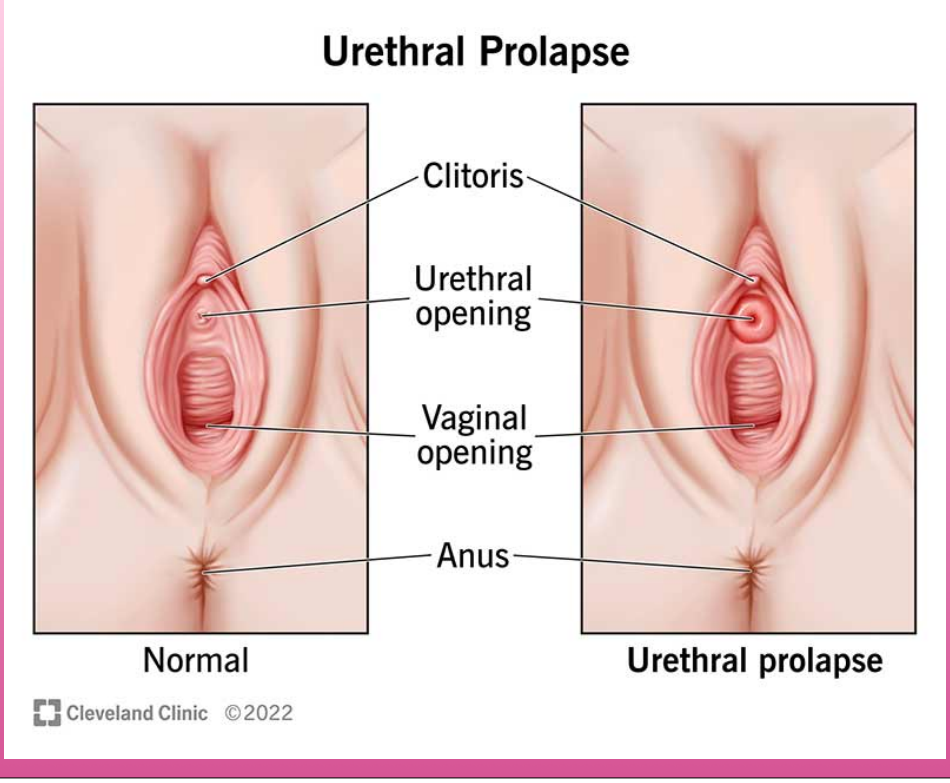
Methods: We performed a systematic literature review of UTI reduction secondary to topical estrogen utilization in postmenopausal female patients. The cost per UTI was determined based on published Medicare spending on UTI per beneficiary, weighted on reported likelihood of complicated and resistant infections. For a patient with recurrent infections, topical estrogen therapy reported on average can reduce infections from 5 to 0.5 to 2 times per person per year.

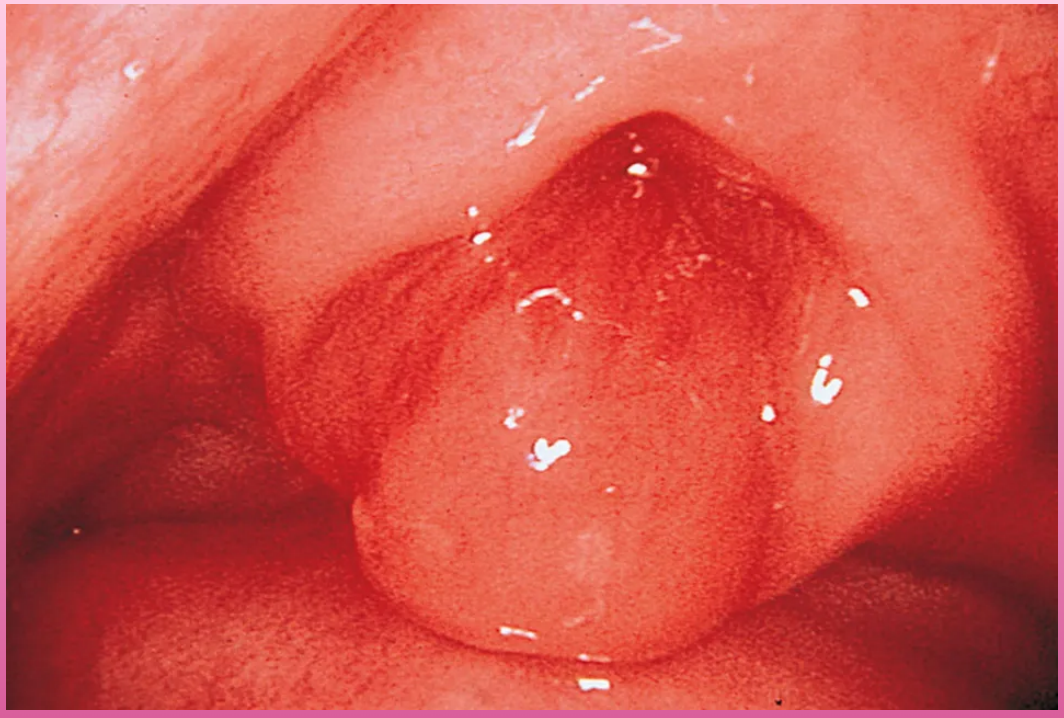
Results: At a calculated cost per UTI of $1222, the reduction in UTI spending can range between $3670 and $5499 per beneficiary per year. Per-beneficiary spending on topical estrogen therapies was $1013 on average ($578-$1445) in 2020. After including the cost of the therapy, overall cost savings for topical estrogen therapies were $1226 to $4888 annually per patient.

Conclusions: Topical estrogens are a cost-conscious way to improve the burden of UTI on postmenopausal women with the potential for billions of dollars in Medicare savings. System-wide efforts should be made to have these therapies available as prophylaxis for postmenopausal patients and to ensure they are affordable for patients.

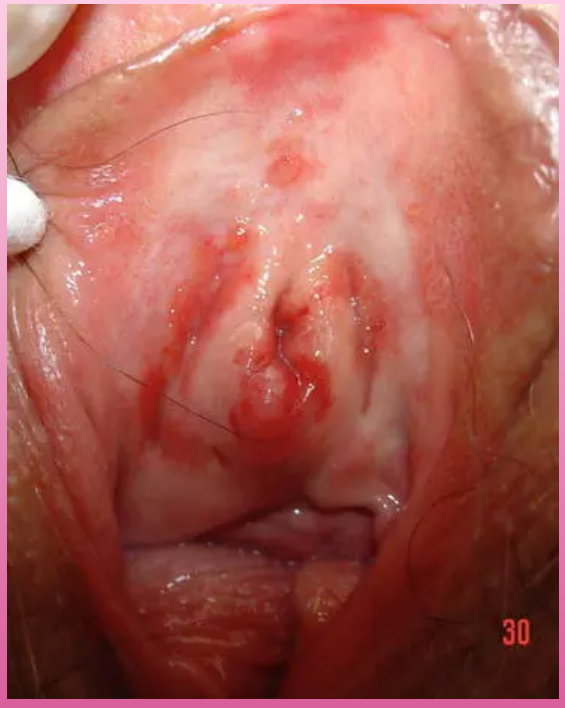
Keywords: cost; economic; menopause; topical estrogen; urinary tract infection.

Houston CG, Azar WS, Huang SS, Rubin R, Dorris CS, Sussman RD. A Cost Savings Analysis of Topical Estrogen Therapy in Urinary Tract Infection Prevention Among Postmenopausal Women. Urol Pract. 2024 Mar;11(2):257-266. doi: 10.1097/UPJ.0000000000000513. Epub 2023 Dec 28. PMID: 38154005.

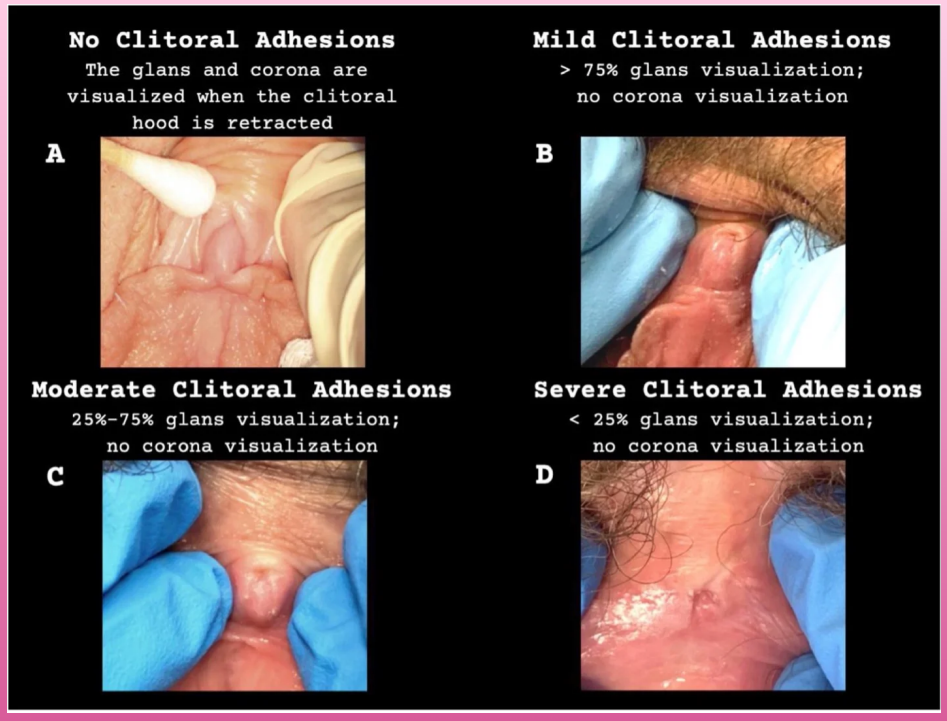




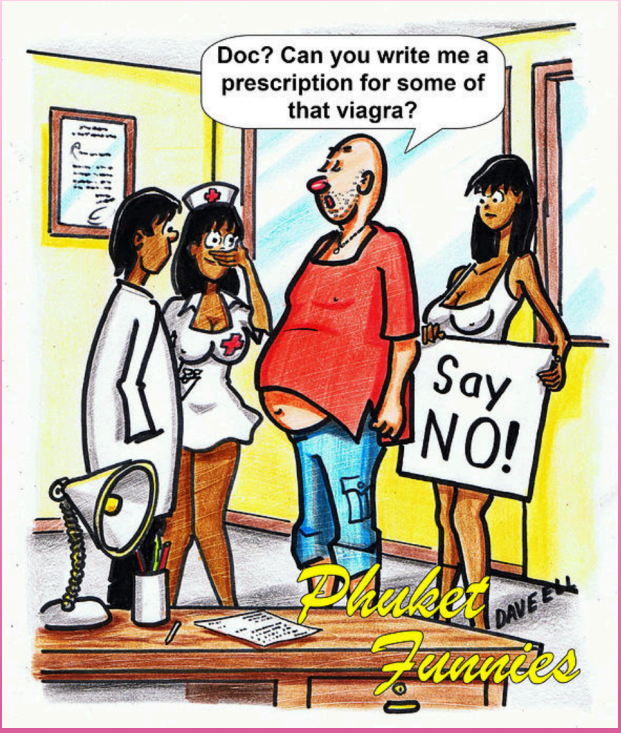
https://obgynkey.com/benign-gynecologic-lesions-vulva-vagina-cervix-uterus-oviduct-ovary-ultrasound-imaging-of-pelvic-structures/



https://obgynkey.com/vulvar-pain-after-the-menopause/



https://www.rachelrubinmd.com/post/new-research-on-clitoral-adhesions



VIAGRA
by DAVE ELL

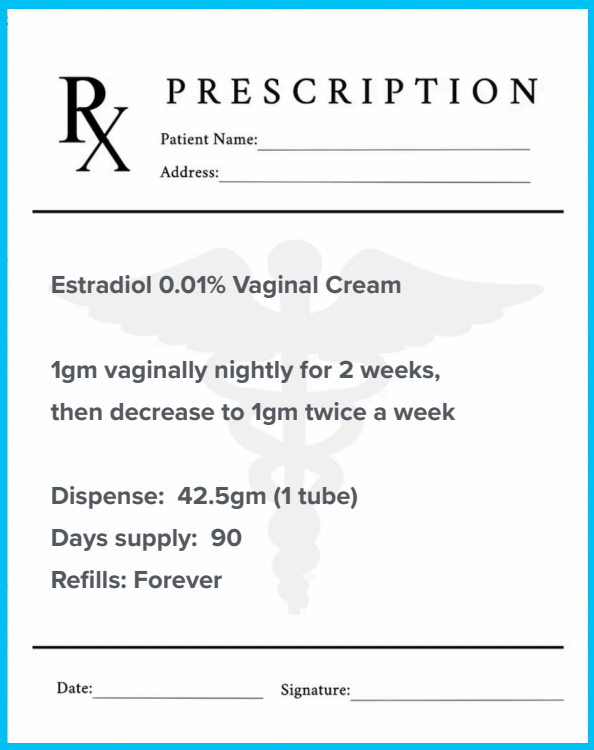
https://render.fineartamerica.com/images/rendered/social-media/8113965?domainId=12

Mode	Cream	Cream	Ring	Insert/Tablet	Insert
Brand names	Premarin	Estrace	E-string	Imvexxy, Yuvafem, Vagifem	Intrarosa
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

https://www.rachelrubinmd.com/

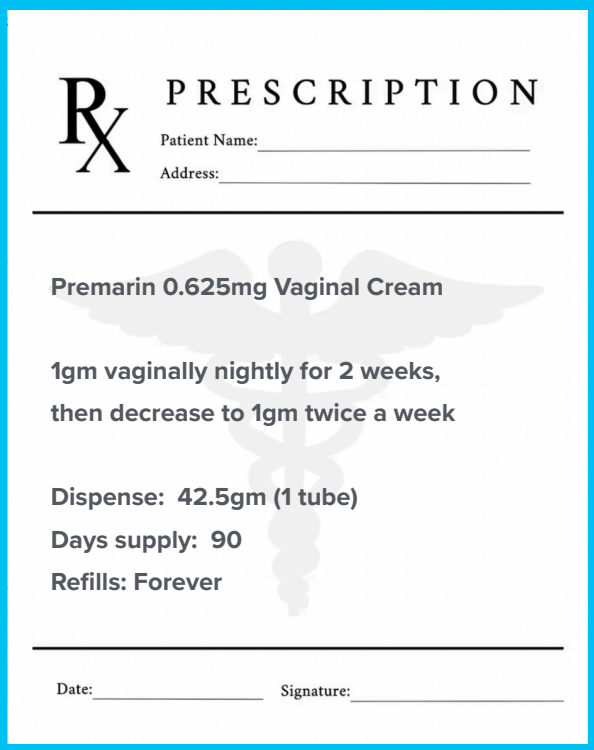
ESTRADIOL 0.01% CREAM

- Estrace brand name
- 17 B-Estradiol 0.01%
- Generic
- Isomolecular to our own Estradiol
- Using this for a year is the equivalent of 1-2 birth control pills worth of estrogen
- Comes with one applicator
- Can use finger
- Also apply a smidge to the vulva with each use
- Cost Plus, Good Rx



CONJUGATED EQUINE ESTROGEN 0.625MG

- Premarin brand name
- Equine Estrogen 0.625mg
- Not generic
- Using this for a year is the equivalent of 1-2 birth control pills worth of estrogen
- Comes with one applicator
- Can use finger
- Also apply a smidge to the vulva with each use



ESTRADIOL 10MCG PILL INSERT

- Vagifem/Yuvafem branded generic names
- 17 B Estradiol 10mcg
- Pill with an applicator
- Comes in boxes of 8
- Consider adding some additional Estrogen cream to the vulva

Rx 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: _____

IMVEXXY 4MCG OR 10MCG

- 17 B Estradiol 4mcg or 10mcg
- No applicator
- Has a little lubricant in it
- Use BlinkRx for automatic coupon card
- Comes in starter packs of 18 gels and maintenance packs of 8 gels
- Consider adding some additional Estrogen cream to the vulva

Rx PRESCRIPTION

Patient Name: _____

Address: _____

Estradiol 4mcg or 10mcg soft gel Insert

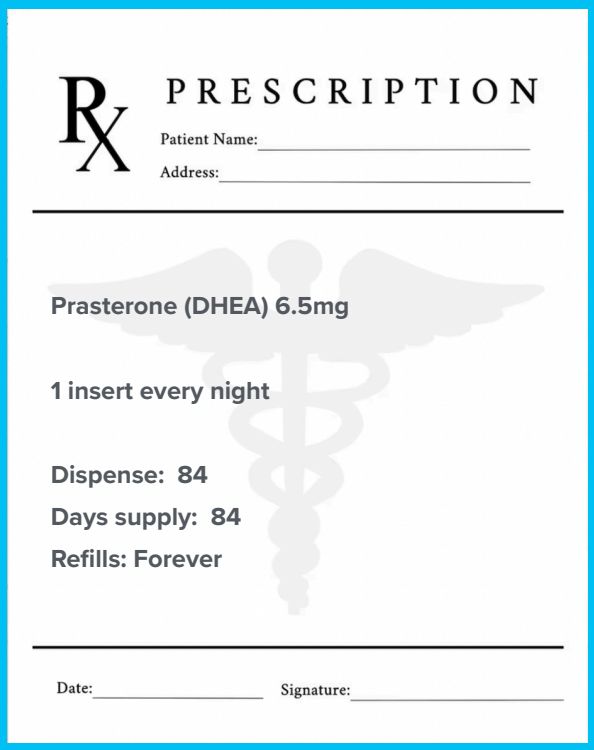
1 insert vaginally nightly for 2 weeks,
then 1 insert twice a week

Dispense: First fill - 18 inserts
Subsequent refills - 24 inserts
Days supply: 90
Refills: Forever

Date: _____ Signature: _____

INTRAROSA 6.5MG

- DHEA 6.5mg and Palm Oil
- Is converted to Estradiol and Testosterone in the cells of the Vagina and vulva
- Comes in boxes of 28
- Comes with an applicator for each insert
- Intrarosa savings program
- Can apply for a prior authorization
- $85/month at Costco

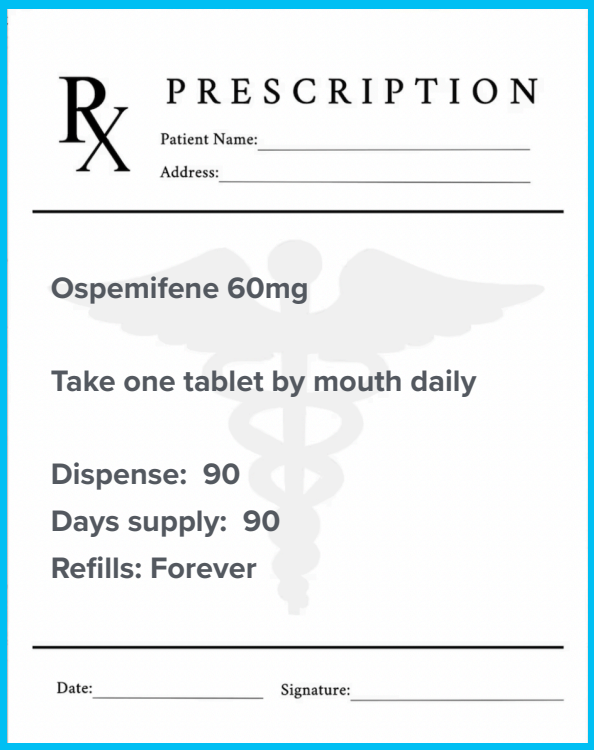


ESTRING 2MG

- 17 B Estradiol 2mg
- 7.5mcg/24 hours
- BlinkRx for best price
- Great option for patients in nursing care facilities, with dementia or with poor dexterity
- $500 on Cost Plus pharmacy

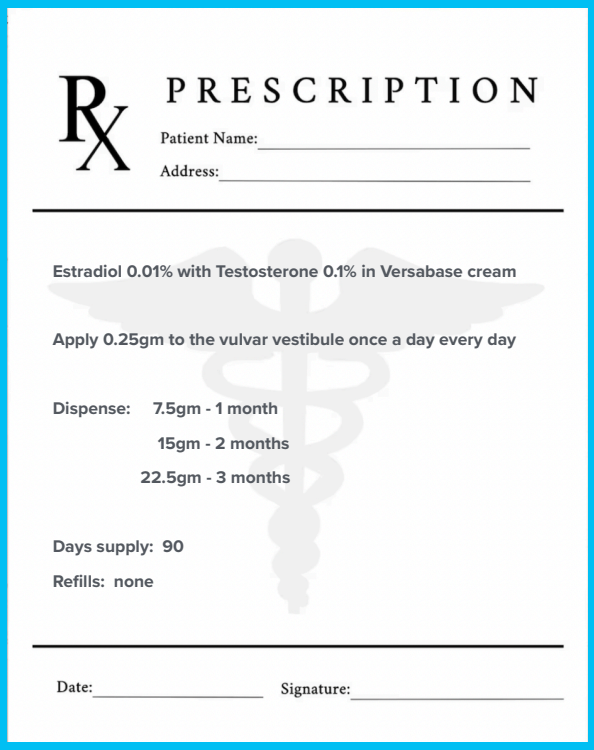
OSPEMIFENE 60MG

- Osphena brand name
- Selective Estrogen Receptor Modulator
- Only oral option
- Systemic so may have side effects
- D/C 4-6 weeks before surgery for VTE risk
- Can cause endometrial hyperplasia and increased risk of VTE



ESTRADIOL 0.01% + TESTOSTERONE 0.1% CREAM

- Good option if patient has tried topical estrogen treatment and still having symptoms
- Must use compounding pharmacy
- Around $80 for a 3 months supply

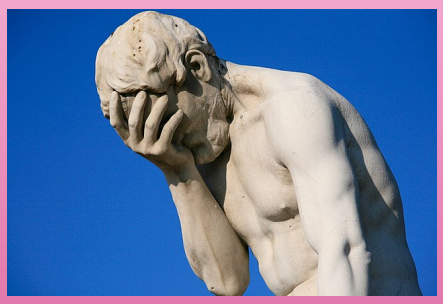


GSM TREATMENT

- These treatments address the root cause
- You may have early relief but takes 8 weeks for maximal benefit
- Many women on systemic hormones also need vaginal/vulval local treatment
- Don’t give up, if not happy with the results then change the delivery system
- Environment is going to become more and more acidic and microbiome normalizes
- Progesterone is not needed for endometrial protection with local Estrogen treatments

FDA CLASS LABELING

- Black Box Warning for increased risk of:
  - Endometrial Cancer
  - Invasive Breast Cancer
  - Stroke
  - DVT
  - Pulmonary Embolism
  - Myocardial Infarction
  - Probable Dementia



https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/020216s073s074s075lbl.pdf

IS 1% HYDROCORTISONE = ORAL PREDNISONE?

ESTRACE® Cream
(estradiol vaginal cream USP 0.01%)

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS, BREAST CANCER and PROBABLE DEMENTIA

Estrogen-Alone Therapy

Endometrial Cancer

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding [see **WARNINGS, Malignant Neoplasms, Endometrial Cancer**].

Cardiovascular Disorders and Probable Dementia

Estrogen-alone therapy should not be used for the prevention of cardiovascular disease or dementia [see **CLINICAL STUDIES** and **WARNINGS, Cardiovascular Disorders**, and **Probable Dementia**].

The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 7.1 years of treatment with daily oral conjugated estrogens (CE) [0.625 mg]-alone, relative to placebo [see **CLINICAL STUDIES** and **WARNINGS, Cardiovascular Disorders**].

The WHI Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with daily CE (0.625 mg) -alone, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women [see **CLINICAL STUDIES** and **WARNINGS, Probable Dementia** and **PRECAUTIONS, Geriatric Use**].

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and other dosage forms of estrogens.

Estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

Estrogen Plus Progestin Therapy

Cardiovascular Disorders and Probable Dementia

Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia [see **CLINICAL STUDIES** and **WARNINGS, Cardiovascular Disorders**, and **Probable Dementia**].

PATIENTS WITH BREAST CANCER

- GSM is the leading cause of sexual dysfunction among breast cancer survivors
- 4 million breast cancer survivors in the US
- Cohort study - no significant difference in recurrence risk within 5 years between breast cancer survivors in those with and without local estrogen therapy
- Studies show systemic absorption is not above menopausal range
- Same restuls in women with hx ER+ breast cancer
- Increased risk of breast cancer recurrence with concurrent use of an aromatase inhibitor and vaginal estrogen

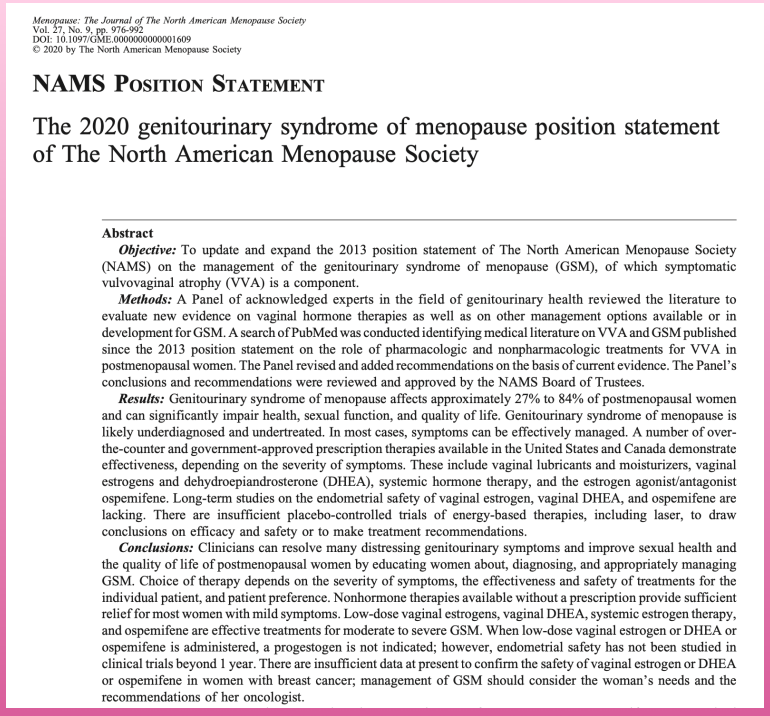
Agrawal P, Singh SM, Able C, Dumas K, Kohn J, Kohn TP, Clifton M. Safety of Vaginal Estrogen Therapy for Genitourinary Syndrome of Menopause in Women With a History of Breast Cancer. Obstet Gynecol. 2023 Sep 1;142(3):660-668. doi: 10.1097/AOG.0000000000005294. Epub 2023 Aug 3. PMID: 37535961.

PATIENTS WITH BREAST CANCER

ASCO GUIDELINES 2018

- Treatment should include a discussion on:
  - Eradicate potential irritants
  - Regular use of a non-hormonal moisturizer
  - Lubricant for sexual activity
  - Pelvic floor physical therapy
  - Patients not responsive to non-hormonal therapies should be offered low-dose vaginal estrogen or dehydroepiandrosterone (DHEA) after discussing the potential risks and benefits of treatment

https://ascopubs.org/doi/10.1200/EDBK_390442
Santen RJ, Mirkin S, Bernick B, Constantine GD. Systemic estradiol levels with low-dose vaginal estrogens. Menopause. 2020 Mar;27(3):361-370. doi: 10.1097/GME.0000000000001463. PMID: 31794498; PMCID: PMC7050796.



Menopause: The Journal of The North American Menopause Society
Vol. 27, No. 9, pp. 976-992
DOI: 10.1097/GME.0000000000001609

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 over-the-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

IN SUMMARY

- This will happen to almost all women, apart from the occasional unicorn
- We need to ask about it and examine our patients when doing paps
- Stopping paps does not mean stopping visual inspection once a year
- Costs the country billions of dollars a year
- Causes women many, many years of suffering, often in silence
- Cheap, safe and effective
- Use Cost Plus, Good Rx, Coupons if needed
- Your patients will love and appreciate you for this
- Urologist Rachel Rubin MD has a great YouTube channel
- ISSWSH - International Society for Study of Women's Sexual Health

THE END