43rd Annual Pacific Northwest Update in Ob-Gyn and Women's Heath
Keynote Lecture
November 15, 2019 1:15-2:15

Menopause and Midlife Sexuality: a bit dry but a must have conversation

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Learning Objectives

- Define vulvovaginal atrophy (VVA), and genitourinary syndrome (GSM) and the impact on post-menopausal dyspareunia
- Identify clinician-based & patient-based factors may inhibit the diagnosis of dyspareunia
- Describe clinician counseling approaches to facilitate a discussion about their symptoms
- Discuss the benefits and risks of innovative therapeutic interventions indicated for the management of menopause related dyspareunia including hormonal, non-hormonal and energy-based therapies

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Yes… Even YOUR Mother has Sex: 60 is the New 40

Michelle *O*bama, 55

Brigitte Macron, 66

Diane Sawyer, 73

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Correlates of Sexual Activity in Older Women: MIDUS II

- Not Sexually Active mean age 62.0 (11.8) n=771
- Sexually Active mean age 51.8 (10.9) n=1345
- **Romantic Partner Status best predictor of whether one was sexually active (regardless of age) even for women in their 70s and 80s**
- Sexually active women still sexually satisfied regardless of age or menopause status

Thurston Ann Fam Med 2015, vol 13.

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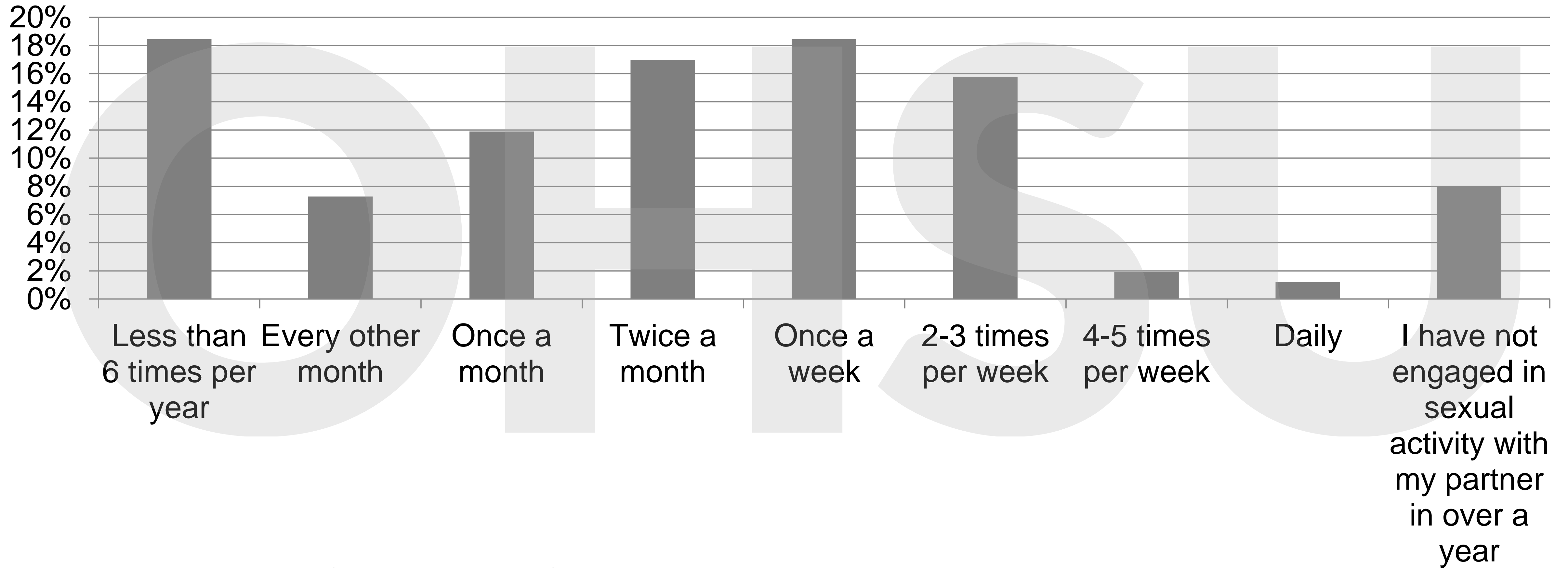
Postmenopausal women are still sexually active



Kingsberg, S. Millheiser L. NAMS Poster 2016

The Impact of Sexual Dysfunction on a Relationship

When sex is good

It adds 15-20% additional value

to a relationship

When sex is bad/non-existent

It plays an inordinately powerful role draining the relationship of all positive value, about 50-70%!

Barry McCarthy 1997 JSMT

Two Most Prevalent Sexual Problems in Postmenopausal Women

- Dyspareunia Due to Genitourinary Syndrome of Menopause (GSM)
- Hypoactive Sexual Desire Disorder (HSDD)

Genitourinary Syndrome of Menopause (GSM)

- A collection of symptoms and signs associated with decreased estrogen and other sex steroids
  - Can involve changes to labia majora/minora, vestibule/introitus, clitoris, vagina, urethra, and bladder
  - Symptoms include, but are not limited to, dryness, pain with sex that may lead to subsequent sexual dysfunction, bladder and urethral symptoms, frequent urinary tract infections, burning, itching, and irritation that are bothersome or distressing.

- Symptomatic vulvovaginal atrophy (VVA) is one component of GSM
  - Treatment of symptomatic VVA may improve all components of GSM

Portman D, Gass M et al, Menopause 2014

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Vulvar and Vaginal Atrophy (VVA)

- Affects up to 69% of postmenopausal women[1,2] and has a detrimental effect on quality of life and sexual function[3,4]

- Most women do not seek medical treatment for their VVA symptoms[3]

Cumming GP, et al. *Menopause Int* 2007;13:79-83. 2. Parish SJ, et al. *Int J Women's Health* 2013;5:437-447. 3. Nappi RE, Kokot-Kierepa M. *Maturitas* 2010;67:233-238.

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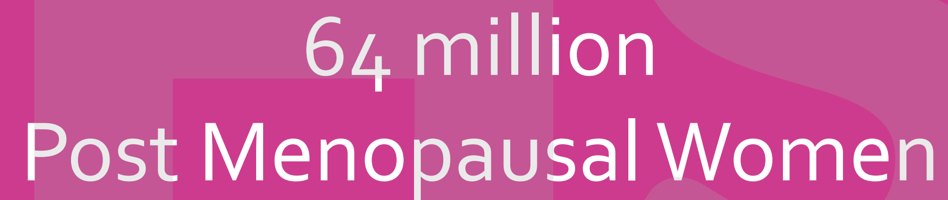

64 million
Post Menopausal Women

Portman DJ, Gass ML. Menopause. 2014;21:1063-1068 ; Kingsberg SA et al. J Sex Med. 2013;10:1790-1799.
Krychman M, Graham S, Bernick B, Mirkin S, Kingsberg SA. J Sex Med. 2017 ; Kingsberg SA, Wysocki S, Magnus L, Krychman ML. J Sex Med. 2013

50%

of postmenopausal women suffer from symptomatic GSM [1,2]

32 million women

1. North American Menopause Society. Menopause. 2013;20(9):888-902.
2. Wysocki S et al. *Clin Med Insights Reprod Health.* 2014;8:23-30

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32 million women

Only 50% (16 million) of women ever seek treatment [2,3]

OTC, over-the-counter.

1. North American Menopause Society. Menopause. 2013;20(9):888-902.
2. Wysocki S et al. *Clin Med Insights Reprod Health.* 2014;8:23-30
3. MacBride MB et al. *Mayo Clin Proc.* 2010;85:87-94.
4. TherapeuticsMD "EMPOWER" Survey, 2016

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25% using OTC Moisturizers And Lubricants [4]

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5. IMS Health Plan Claims (April 2008-Mar 2011).

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7% of Women Treated with Prescription Medication [5]

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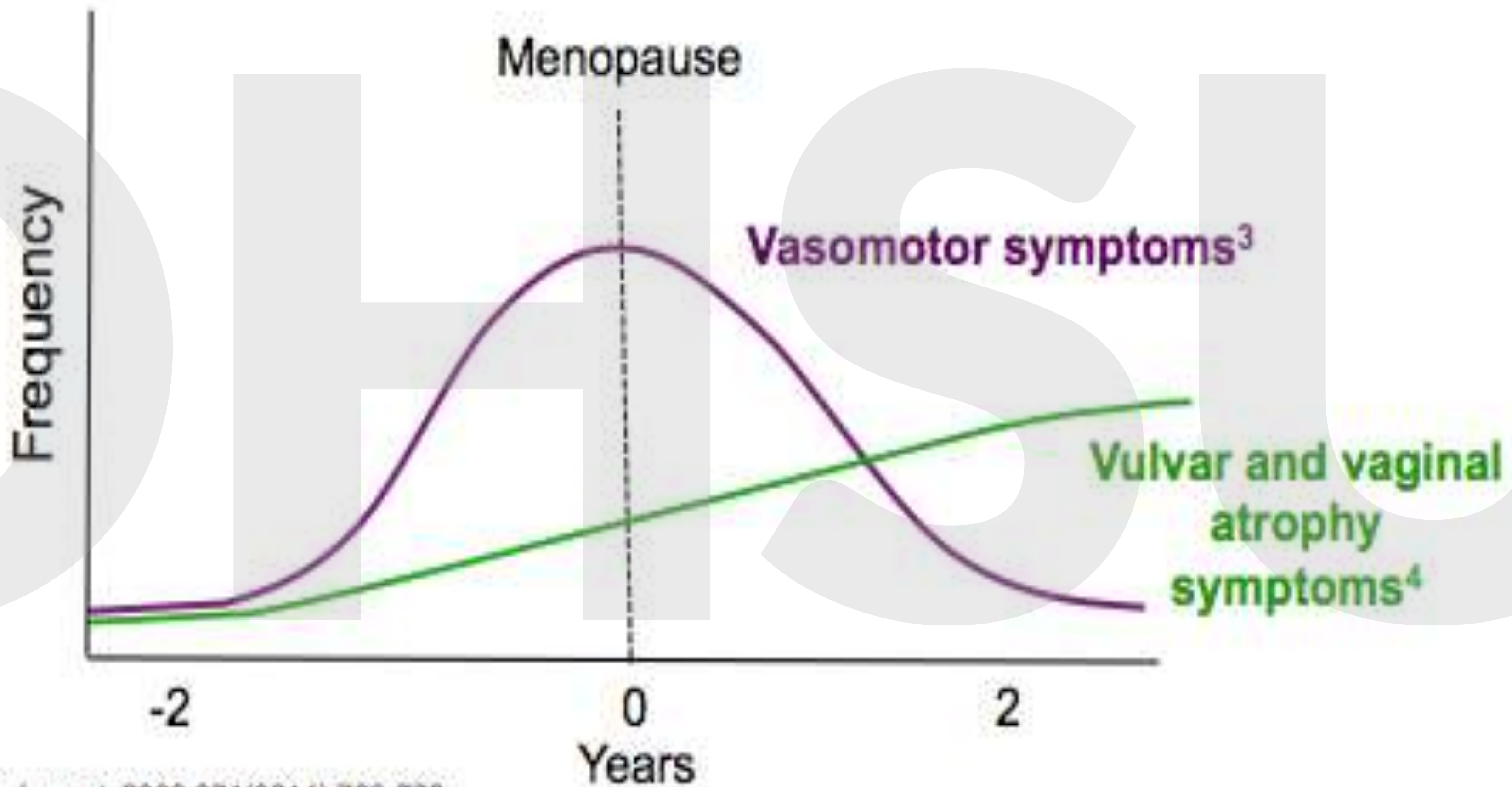
Unmet Need of Women

16 million (50%) Never treated

Onset of Vasomotor Symptoms vs Vulvovaginal Symptoms



1. Nelson HD. *Lancet*. 2008;371(9614):760-770.
2. Bachmann GA, Nevadunsky NS. *Am Fam Physician*. 2000;61(10):3090-3096.
3. Kronenberg F. *Ann N Y Acad Sci*. 1990;592:52-86.
4. Dennerstein L et al. *Obstet Gynecol*. 2000;96(3):351-358.

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U.S. Women Don't Realize VVA Symptoms Are Caused by Menopause

- When women in the survey were asked, in an unaided question, to name the cause of their VVA symptoms:
  - Only 24% of the women attributed their symptoms directly to Menopause
- Of the 76% citing another cause for their VVA symptoms, 33% responded they "Don't Know"

REVIVE, Real Women's Views of Treatment Options for Menopausal Vaginal Changes Survey Kingsberg S, et al. *J Sex Med*. 2013;10

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Suffering in Silence

- Although quite common and bothersome, most women fail to get treatment (~ 93%)[1] due to:
  - Embarrassment[2]
  - Lack of knowledge about VVA[1]
  - Lack of knowledge of approved treatment options[1]
  - Negative attitudes regarding hormone therapy[3]

- Women who do seek treatment are often dissatisfied with the safety, convenience, and efficacy of current approved products.[1]

1. Kingsberg SA et al. *J Sex Med.* 2013;10:1790-1799.
2. Nappi et al. *Maturitas.* 2010;67:233-238.
3. Simon et al. *Menopause.* 2013;20:1043-1048.

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Key Barriers to Patient Treatment

- **Lack of awareness** by patients of symptoms relating to menopause[2]
- **Lack of discussion** regarding symptoms with HCPs[2]
- **Self-medication** with OTC lubricants/moisturizers and/or herbal medications[17]
- **Dissatisfaction with delivery systems** (e.g., messy creams)[18]
- Unwillingness to take FDA-approved estrogen therapies due to **"safety concerns"**[5]
- **Discontinuation** after initiation (typically 2-3 months)[18]

5. Wysocki S, Kingsberg S, Krychman M. *Clin Med Insights: Reprod Health* 2014:8 23-30.
17. Al Baghdadi O, Ewies AAA. *Climacteric* 2009;12:91-105
18. Portman D, Shulman L, Yeaw J, et al. *Menopause* 2015;22(11):1197-1203.

Consistent Findings Across Multiple Large Surveys of Women with VVA

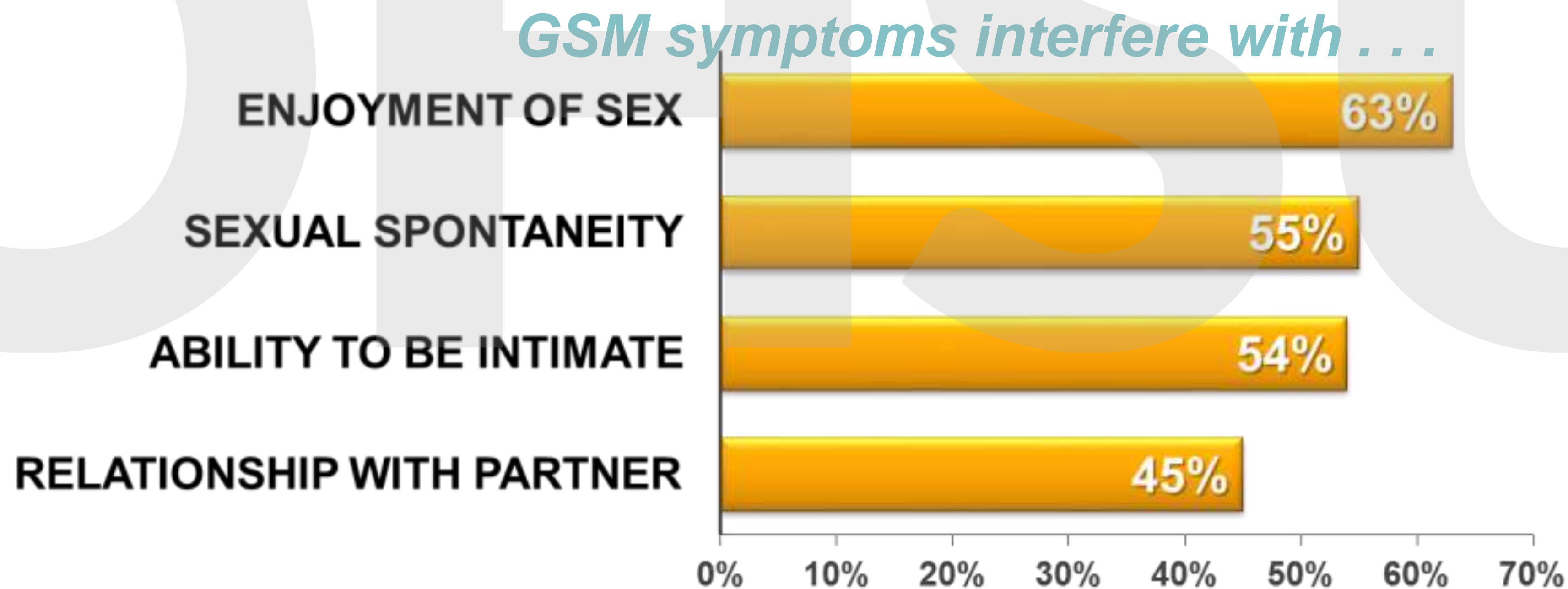
Name / Date	Country	Subjects	Method
VVA Focus Groups 2015	USA	38; with VVA symptoms; 49-74y	Focus Group
VIVA 2010	International / USA	3,520; postmenopausal; 55-65 y	Online survey
CLOSER 2011-12	Europe / N America	4,100; no menstruation for ≥12 mo; 55-65 y	Online survey
REVIVE 2012-14	USA / Europe	3,046/3768 postmenopausal; VVA symptoms; 45-75 y	Online survey
EMPOWER 2016	USA	1,858; with VVA symptoms; ≥45 y	Online survey

CLOSER: Clarifying Vaginal Atrophy's Impact on Sex and Relationship; EMPOWER: Women's EMPOWER survey; REVEAL: Revealing Vaginal Effects at Mid-Life; REVIVE: Real Women's Views of Treatment Options for Menopausal Vaginal Changes; USA: United States of America; VIVA: Vaginal Health: Insight, Views, & Attitudes; Presented at the North American Menopause Society Annual Meeting, October 9, 2015, Las Vegas NV.

. Krychman M, Graham S, Bernick B, Mirkin S, Kingsberg SA. *J Sex Med.* 2017

Impact of GSM Symptoms on Sexual Function (REVIVE)

- Vaginal dryness (55%); dyspareunia (44%); vaginal irritation (37%)



Kingsberg S, et al. *J Sex Med*. 2013;10:1790-1799.

VVA Unmet Need (REVIVE)

- Women reported only 19% of HCPs addressed their sexual life
  - Only 13% raised the issue of VVA symptoms specifically during their checkup
  - 50% of patients think GSM is a natural—and perhaps unavoidable—consequence of aging
  - Others do not associate GSM with menopause
  - 40% of these women expected that their HCP would initiate discussion related to menopausal symptoms

Kingsberg S, Wysocki S, Magnus L, Krychman M. *J Sex Med, 2013*.

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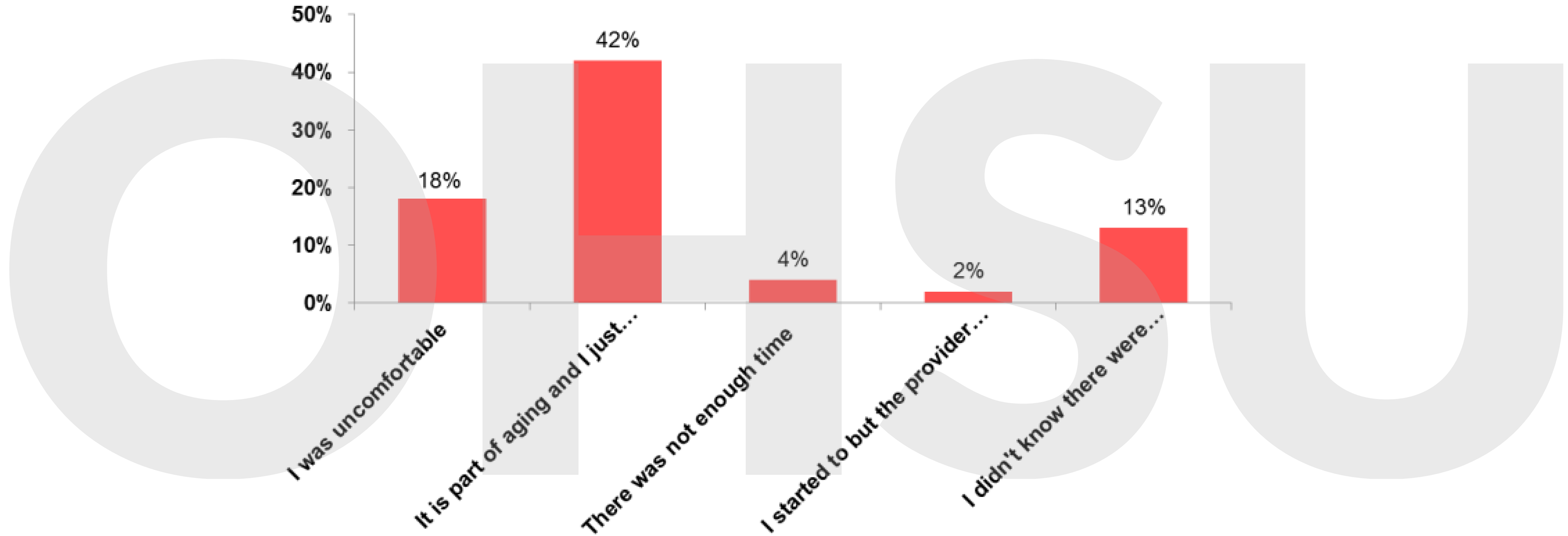
The Women's EMPOWER survey: The Most Common Reasons Why Women Do Not Bring up Pain with Sex



- Thought the symptoms are a part of aging
- Were uncomfortable
- Were not aware of treatments available

Kingsberg S, et al J Sex Med 2017 March 14 (3)

Barriers to Communication, Diagnosis and Treatment and Some Solutions

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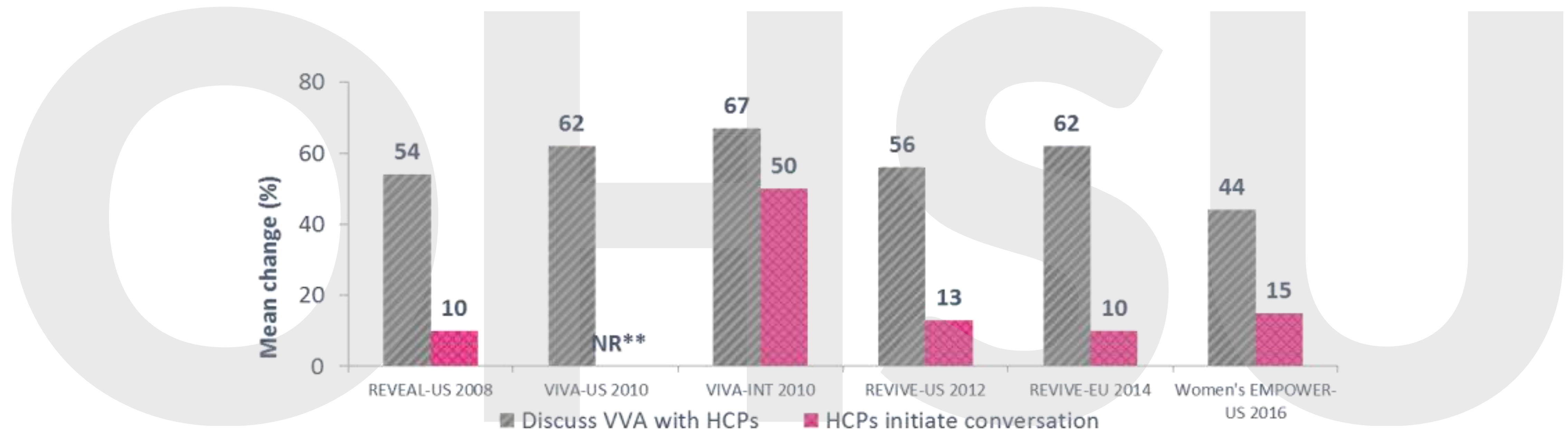
Physician Barriers to Addressing Sexual Health

- Perception it takes too long
- Consider other issues as higher priorities
- HCP embarrassment
- Inadequate knowledge/skills
- Fear of embarrassing patient
- Assume reimbursement is poor
- Few FDA approved treatments

- Korenman, SG, 1998; Brokeman, CPM et al, 1994; Eid JF et al, 2001; Baum, N et al, 1998

HCPs Are Reluctant to Initiate Dialogue With Their Patients regarding Symptoms of Vaginal Atrophy[2*]



studies can be found in specific references cited in Krychman; **NR = not reported

CLOSER: Clarifying Vaginal Atrophy's Impact on Sex and Relationship; EMPOWER: Women's EMPOWER survey; REVEAL: Revealing Vaginal Effects at Mid-Life; REVIVE: Real Women's Views of Treatment Options for Menopausal Vaginal Changes; USA: United States of America; VIVA: Vaginal Health: Insight, Views, & Attitudes; WVM: Women's Voices in Menopause

. Krychman M, Graham S, Bernick B, Mirkin S, Kingsberg SA. *J Sex Med.* 2017 In Press.

Screening for VVA and Dysparuenia

- Normalize/universalize conversations about sexual health issues
- Start with open-ended **ubiquity-style question**
  - "Many women after menopause start to develop sexual problems such as pain with sex and/or dryness. What changes have you noticed?
  - Open, non-defensive body posture
  - Sit and maintain eye contact
  - Avoid nervous gestures

Open-Ended Questions

- HCPs ask ≈1 question/min; >90% are closed-ended
- Actual time for patient to tell their story

  Max 150 seconds, most <60 seconds

Open-ended questions improve:

- assessment of functional impairment
- adherence
- patient satisfaction

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Discomfort with Silence

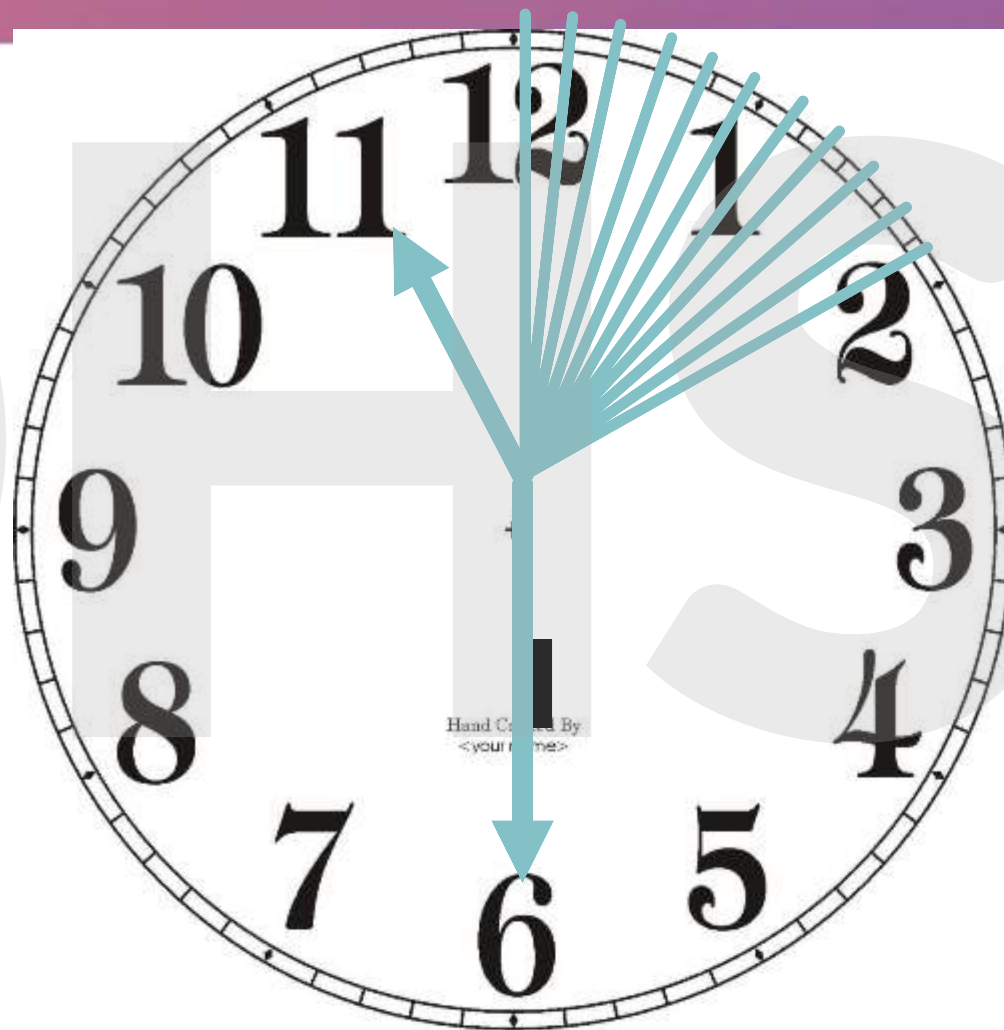
On average, how quickly is a patient interrupted?

Allow Patients to Talk

***Research shows** that, on average **patients are interrupted** by physicians every **12-23 seconds** during a consultation*

- Rhoades et al 2001

The Power of Silence



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Basic Screening for Sexual Function

Legitimize importance of assessing sexual function; normalize as part of usual history and physical

Are you currently involved in a relationship…sexual ?

Have your partners included men, women or both?
What sexual concerns do you have?

Do you have sexual concerns that you would like to discuss or that have contributed to lack of sexual behavior?

Adapted from Kingsberg S. Sex, Urol Clin N Am. 2000;34:497-506.

Office Based Counseling for Sexual Problems: Follow PLISSIT Model

Permission to talk about sexual issues, reassurance and empathy

Limited **I**nformation

e.g., education about genital anatomy or educational resources

Specific **S**uggestions

e.g., use of lubricants, altering position

Intensive **T**herapy

e.g., referral for psychotherapy/sex therapy

Annon, 1976

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FIRST SUMMARY

- GSM and dyspareunia is common but underdiagnosed and undertreated
- Initiate the discussion with ALL of your patients
- Many safe and effective treatments

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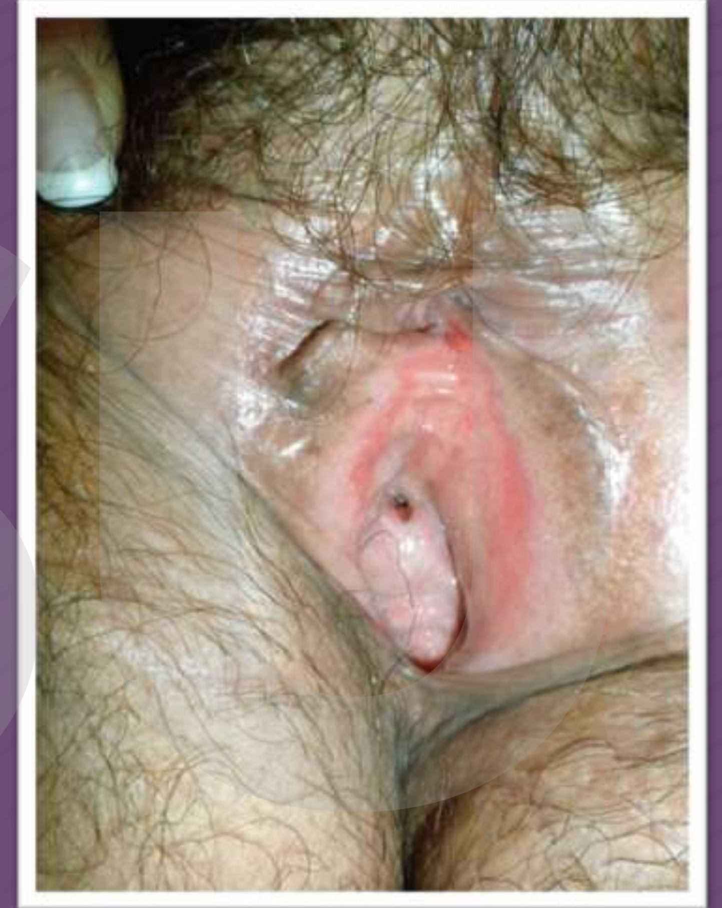
Beyond Sandpaper Sex…or Die Trying

GSM Symptoms

- Irritation
- Burning
- Itching
- Increased discharge or odor
- Dyspareunia
- **Vaginal and vulvar dryness**
- LUTS—dysuria, frequency, urgency



Bachmann G, et al. *Up to Date.* 2012; Grady D. *N Engl J Med.* 2006; Kingsberg S, et al. *Int J Women's Health*. 2009; Portman DJ et al JSM 2014

Gynecological Cancers and Breast Cancer

- **Vaginal atrophy** is often result of radiotherapy, chemotherapy and/or hormonal manipulation
- Majority of tumors are hormone-sensitive

Limited data on vaginal estrogens in women with hormone-sensitive cancers

Non-hormonal therapies preferred but often ineffective

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Vaginal Consequences of Estrogen Deficiency

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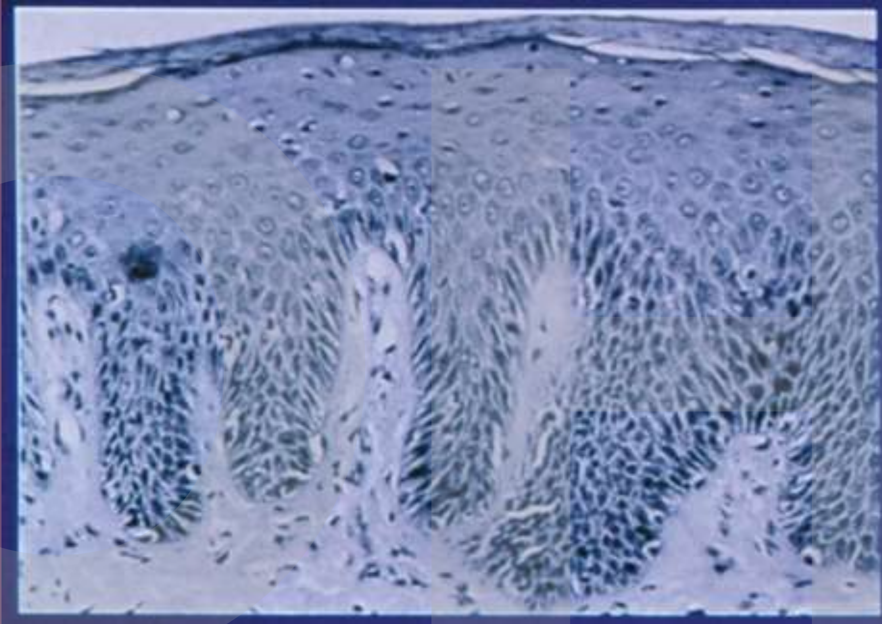
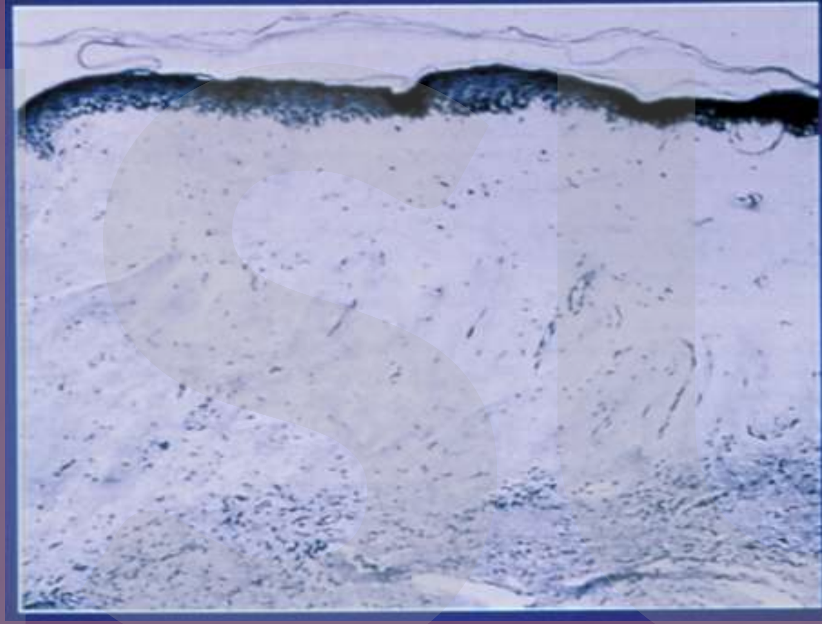
Vaginal Histology



Premenopause

Epithelium well-estrogenized,multi-layered with good blood supply, superficial cells rich in glycogen



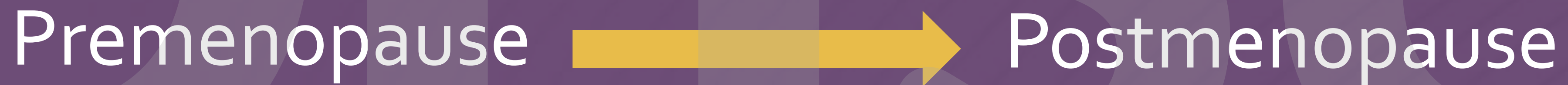
Postmenopause

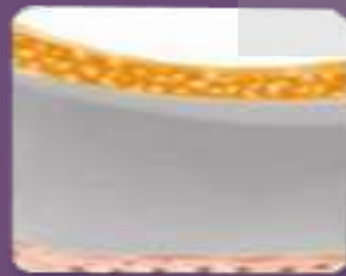
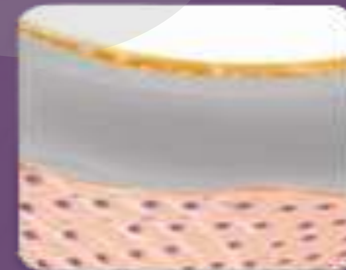
Estrogen-deficiency atrophy with marked thinning of epithelium, blood supply reduced, and loss of glycogen

Vaginal Maturation Index

Postmenopausal vaginal epithelium:

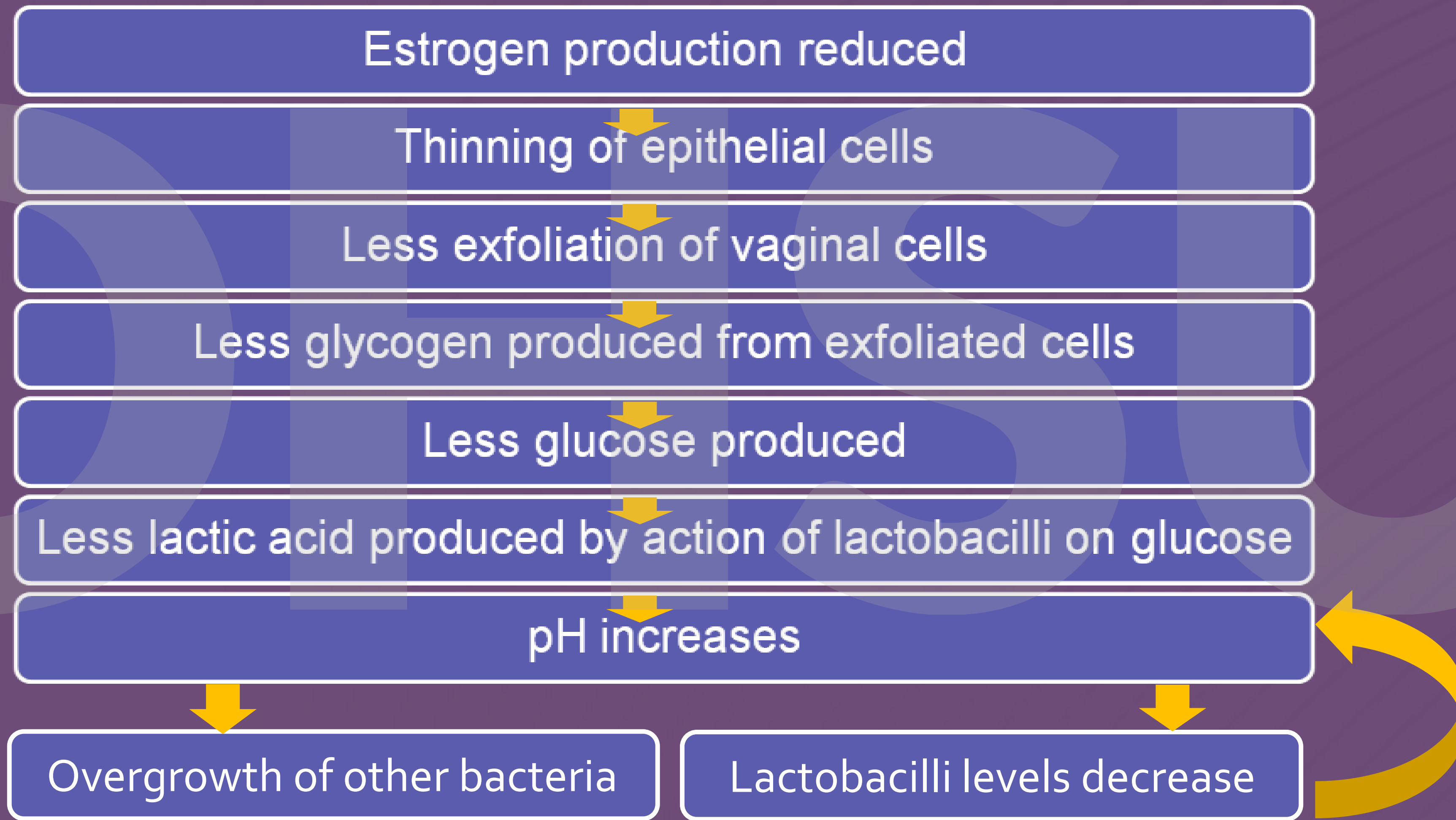
- Superficial cells decreased
- Parabasal cells increased



	Premenopause		Postmenopause	
Superficial cells		15%		1%
Intermediate cells		80%		60%
Parabasal cells		5%		39%

Freedman M. Menopause Manag. 2008;17:9-13. Reprinted with permission.

Mechanism of Vulvovaginal Atrophy



MacBride M, et al. *Mayo Clin Proc.* 2010; Krychman ML. *Medscape Ob/Gyn.* 2007.

patient DS G2P2

- Age 53 pH 4-4.5 E2=51
- Age 55 pH 5-5.5 E2=17
- Age 56 pH 5.5 amenorrheic 2yr

Courtesy Dr. M A Freedman

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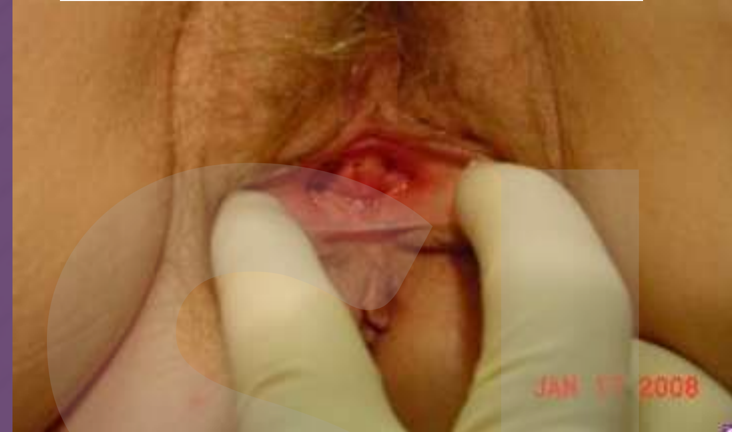
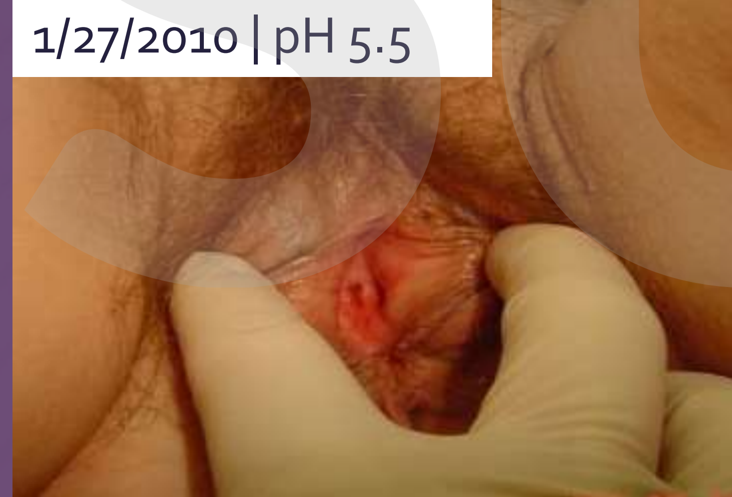
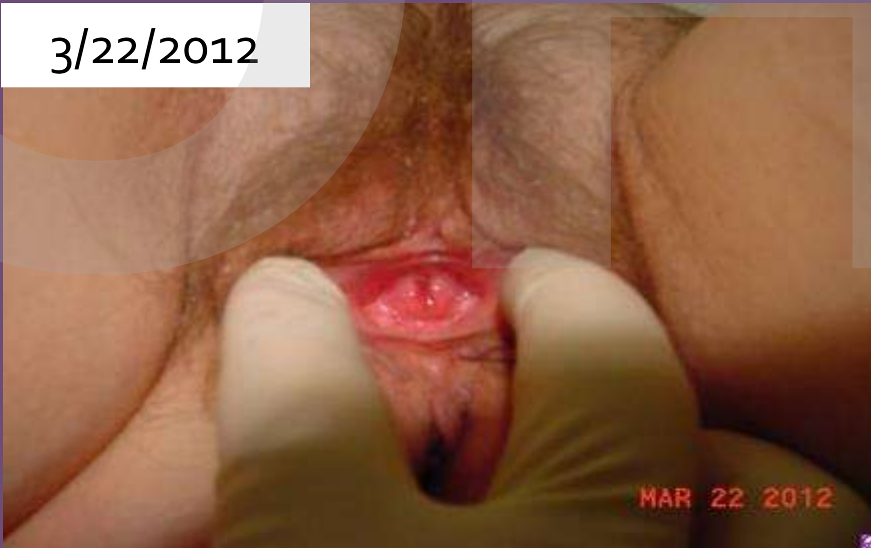


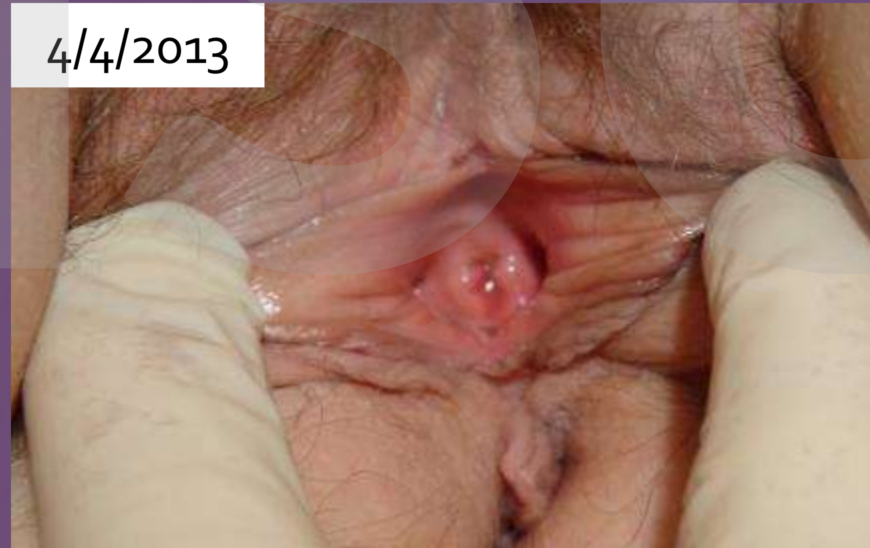


(Courtesy M Freedman)

1/27/2010

3/15/2011
MAR 15 2011

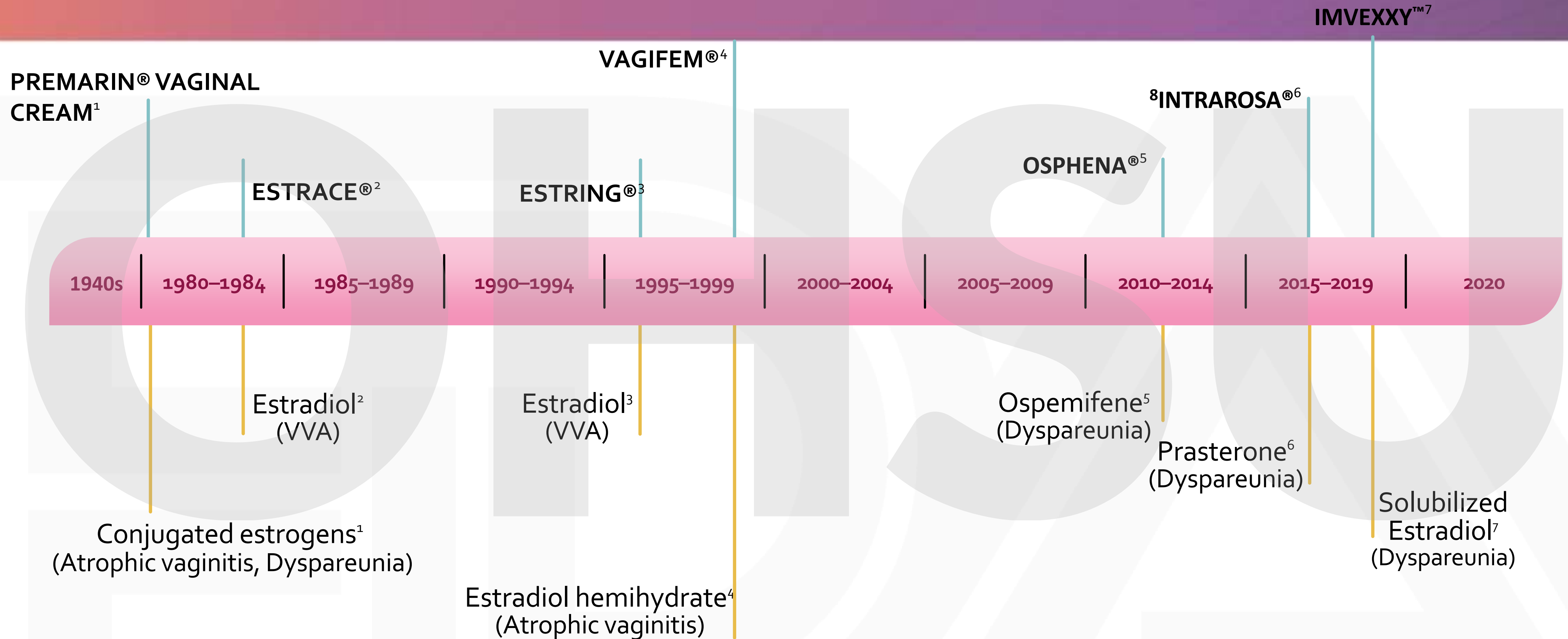

3/22/2012
MAR 22 2012


4/4/2013

FDA Approved Options Dyspareunia/Vulvovaginal Atrophy

- Local estrogen:
  - vaginal cream, vaginal ring, vaginal pill
- Ospemifene
- DHEA prasterone
- Solubized estradiol

FDA-Approved Treatment Options



PREMARIN, ESTRACE, ESTRING, VAGIFEM, OSPHENA and INTRAROSA are registered trademarks of their respective owners. IMVEXXY is a trademark of TherapeuticsMD, Inc.

VVA: vulvar and vaginal atrophy

1. Premarin (conjugated estrogens) prescribing information, Pfizer.
2. Estrace (estradiol) prescribing information, Allergan.
3. Estring (estradiol) prescribing information, Pfizer.
4. Vagifem (estradiol) prescribing information, Novo Nordisk Inc.
5. Osphena (opemifene) prescribing information, Duchesnay USA, Inc..
6. Intrarosa (prasterone) prescribing information, AMAG Pharmaceuticals, Inc.
7. IMVEXXY (estradiol) prescribing information, TherapeuticsMD, Inc.

Conveying Risks and Warnings About Vaginal Estrogen Therapy

85%

Aware and concerned about safety issues with hormones

Low-dose vaginal estrogen therapy is safer than systemic therapy

Santoro N, et al. *J Sex Med.* 2009.; Grady D. N Engl J Med. *2006.;* Bachmann G, et al. *Up to Date.* 2012.

NAMS Guidelines 2018

Finder

Sun 1:44 PM

CONSENSUS RECOMMENDATIONS

Management of genitourinary syndrome of menopause in women with or at high risk for breast cancer: consensus recommendations from The North American Menopause Society and The International Society for the Study of Women's Sexual Health

Stephanie S. Faubion, MD, FACP, NCMP, IF,[1] Lisa C. Larkin, MD, FACP, NCMP, IF,[2] Cynthia A. Stuenkel, MD, NCMP,[3] Gloria A. Bachmann, MD,[4] Lisa A. Chism, DNP, APRN, BC, NCMP, CSC, FAANP,[5] Risa Kagan, MD, FACOG, CCD, NCMP,[6] Andrew M. Kaunitz, MD, FACOG, NCMP,[7] Michael L. Krychman, MD, FACOG, MPH, IF,[8] Sharon J. Parish, MD, IF, NCMP,[9] Ann H. Partridge, MD, MPH,[10] JoAnn V. Pinkerton, MD, FACOG, NCMP,[11] Tami S. Rowen, MD, MS,[12] Marla Shapiro, CM, MDCM, CCFP, MHSC, FRCPC, FCFP, NCMP,[13] James A. Simon, MD, CCD, NCMP, IF, FACOG,[14] Shari B. Goldfarb, MD,[15] and Sheryl A. Kingsberg, PhD[16]

Abstract

The objective of The North American Menopause Society (NAMS) and The International Society for the Study of Women's Sexual Health (ISSWSH) Expert Consensus Panel was to create a point of care algorithm for treating

NAMS Guidelines

Individualize treatment based on symptoms, QoL and risk for recurrence

First Line Therapy

- **Moisturizers, lubricants, Pelvic floor PT, dilators**
- Local hormones if OK with oncologist
- Compounded vaginal estriol and testosterone **not recommended**
- Ospemifene **not studied** in women at hi risk for breast cancer

Women at high risk for breast cancer (BRCA etc)

- Local hormones reasonable for those who have failed non-hormone treatment
- Observational data suggest no increased risk of breast cancer

NAMS Guidelines for Breast Cancer Survivors

ER+ breast cancer on tamoxifen

- With severe symptoms, local hormone at low risk for recurrence

ER + breast cancer on AI

- Severe symptoms, may consider local hormones or switch to tamoxifen

Triple negative breast cancer

- Local hormone reasonable but data lacking

Women with metastatic disease

- QoL, intimacy, comfort may be priority
- Use of local hormone may be viewed differently in women with limited survival

Treatment	Product Name	Initial Dose	Maintenance Dose
Vaginal cream 17 Beta Estradiol Conjugated Estrogen	Estrace Premarin	0.5-1gm/d x 2 wk	0.5-1 gm 1-3x/wk
Vaginal Inserts Estradiol 17 Beta estradiol soft gel DHEAS prasterone	Vagifem/Yuvafem Imvexxy Intrarosa	10ug/d x 2 wk 4,10 or 25 ug/d x 2 wk 6.5 mg/d	1 twice/wk 1 twice/wk 1/d
Vaginal Ring	Estring	7.5ug/day	90 days
SERM Ospemifene	Osphena	60 mg/d	60 mg/d

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Ospemifene and Dyspareunia Associated with GSM

- Multicenter phase 3 randomized, double-blind 12-week efficacy and safety study
- 605 women 40-80 yrs (mean age 58) with self-reported most bothersome symptom MBS of dyspareunia
  - Ospemifene 60 mg po daily (n = 303) vs placebo (n = 303)
- Co-primary endpoints
  - pH, parabasal, superficial cells
  - Change in severity using VVA symptom questionnaire of MBS of dyspareunia

Portman DJ, Bachman GA, Simon JA. *Menopause* 2013;20(6):1-8.

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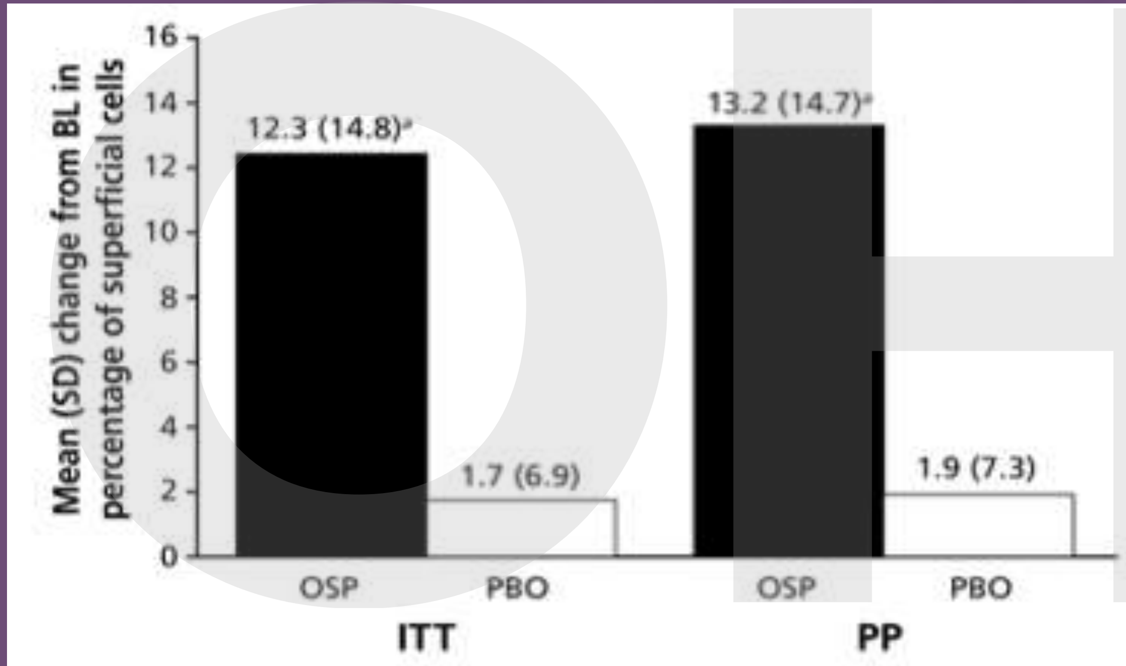
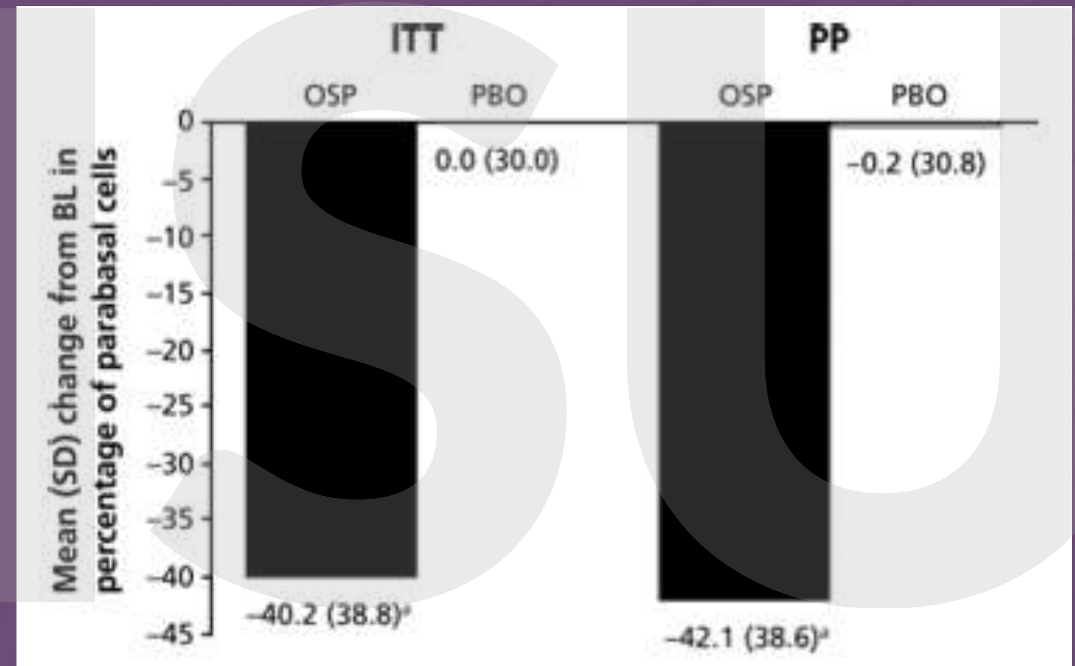
Ospemifene and Dyspareunia Associated with VVA

Change in baseline to week 12



Superficial Cells



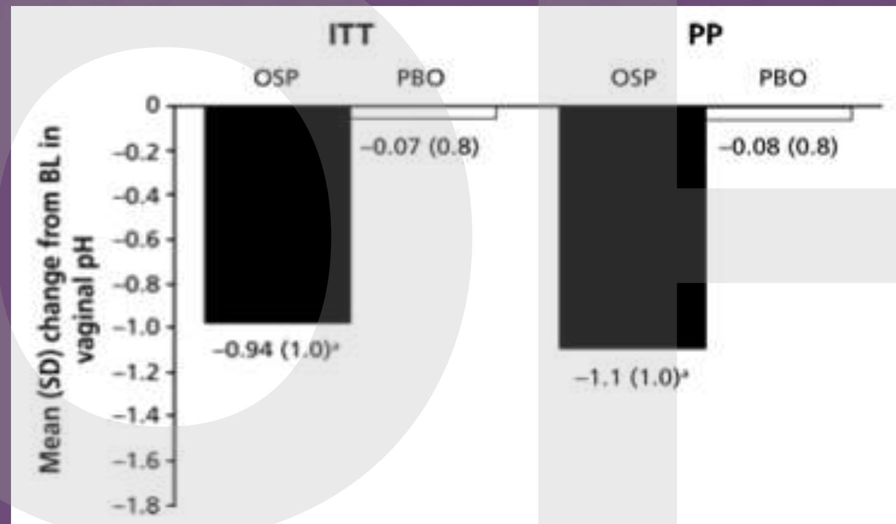
Parabasal Cells

P< 0.0001 versus placebo for all

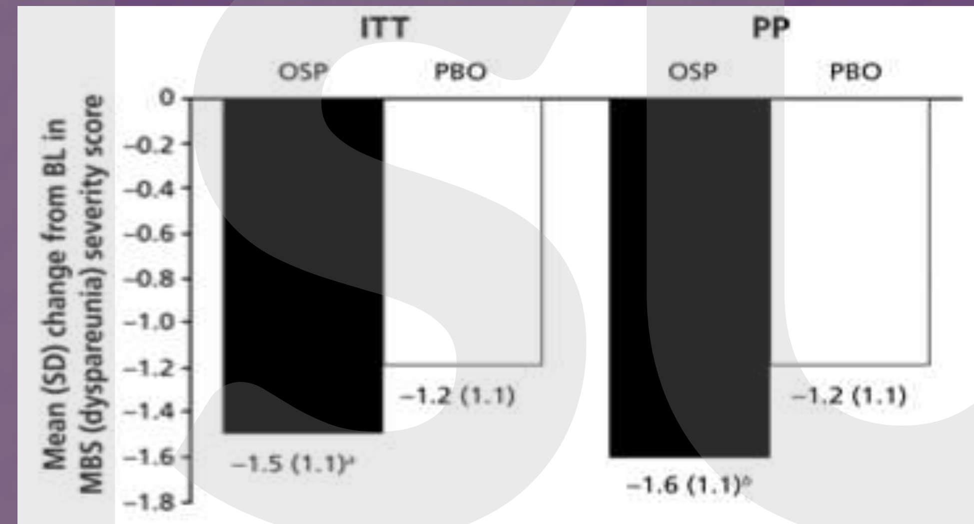
Portman DJ, Bachman GA, Simon JA. *Menopause* 2013;20(6):1-8.

Ospemifene and Dyspareunia Associated with VVA

Change in baseline to week 12



pH



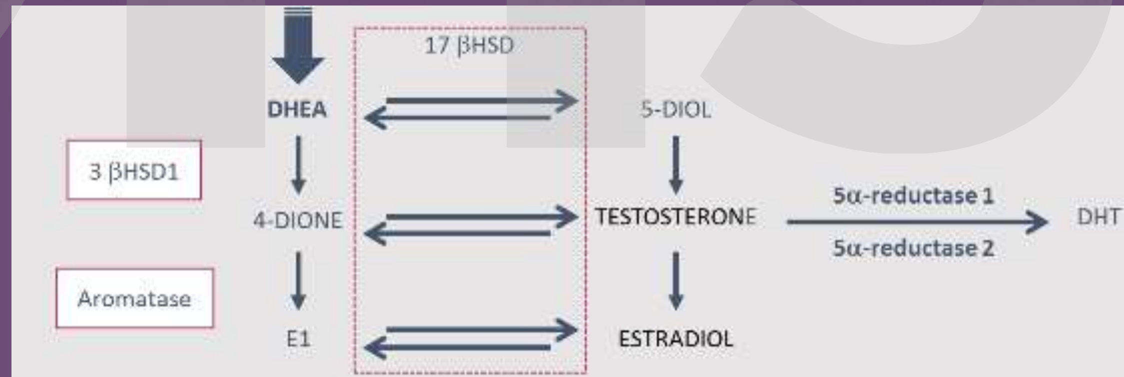
MBS Dyspareunia

P< 0.0001 versus placebo for all

Portman DJ, Bachman GA, Simon JA. *Menopause* 2013;20(6):1-8.

INTRAROSA (prasterone) Vaginal Inserts: Putative Mechanism of Action

- The mechanism of action of INTRAROSA in postmenopausal women with vulvar and vaginal atrophy is not fully established[1]
- Prasterone is a synthetic form of the inactive endogenous steroid, DHEA
- Prasterone is converted in the body into active androgens and/or estrogens by steroidogenic enzymes such as hydroxysteroid dehydrogenases, 5α-reductases and aromatases[2]



[1]INTRAROSA® Prescribing Information, AMAG Pharmaceuticals, February 2018.
[2]Labrie et al. Menopause 2016;23: 243-256.

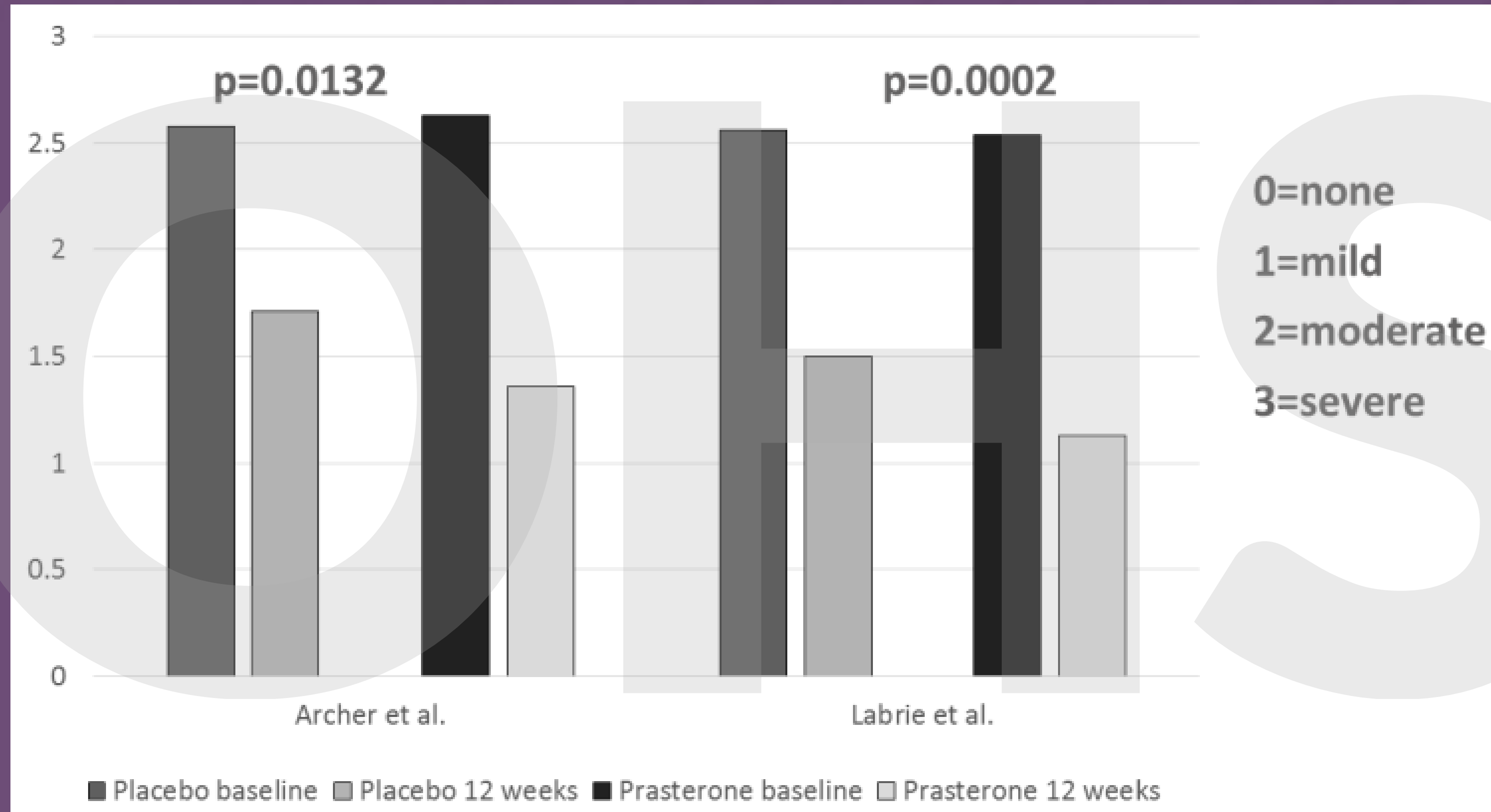
Prasterone Efficacy: 2 Clinical Studies

	Archer et al. [1]	Labrie et al. [2]
# Patients	253	558
Age (mean, range), years	58.6 (40-75)	59.5 (40-80)
Study Length	12 weeks	12 weeks
Randomization	1:1:1 (0.25% prasterone: 0.5% prasterone: placebo)	2:1 (0.5% prasterone: placebo)
Intent-to-treat	All women receiving at least one dose of the study drug or placebo	
Co-primary endpoints (change from baseline to 12 weeks)	% Parabasal cells % Superficial cells Vaginal pH Change in dyspareunia score	

[1] Archer et al. Menopause 2015;22: 950-963.

[2] Labrie et al. Menopause 2016; 23: 243-256.

Significant Decreases in Dyspareunia with Prasterone Vaginal Inserts

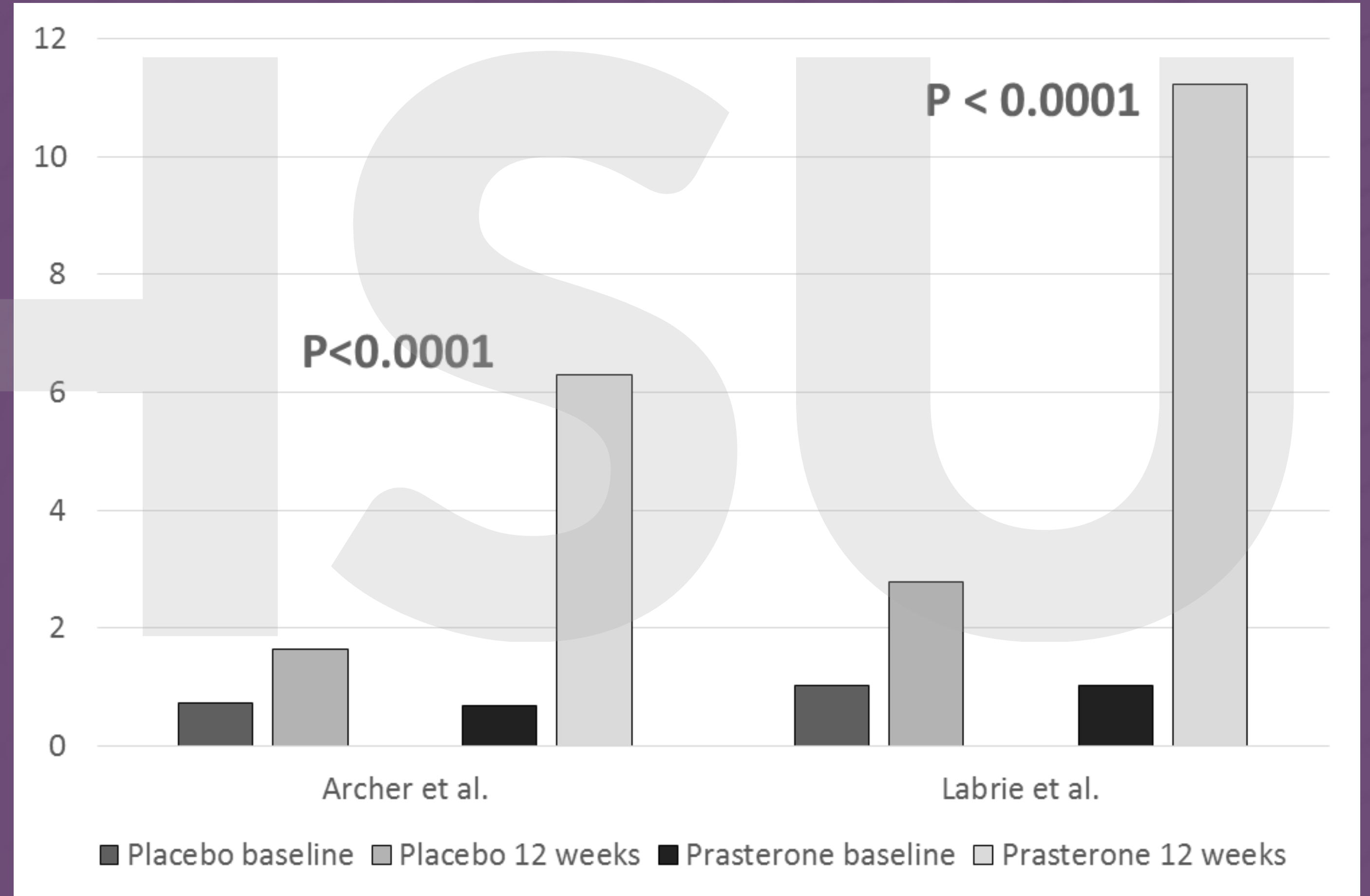


Difference from placebo: Prasterone (Week 12 mean – Baseline mean) – Placebo (Week 12 mean – Baseline mean). p-value calculation: analysis of covariance using treatment as the main factor and baseline value as the co-variate

[1] Archer et al. Menopause 2015;22: 950-963.
[2] Labrie et al. Menopause 2016; 23: 243-256.

Significant Increases in % Superficial Cells with Prasterone Vaginal Inserts

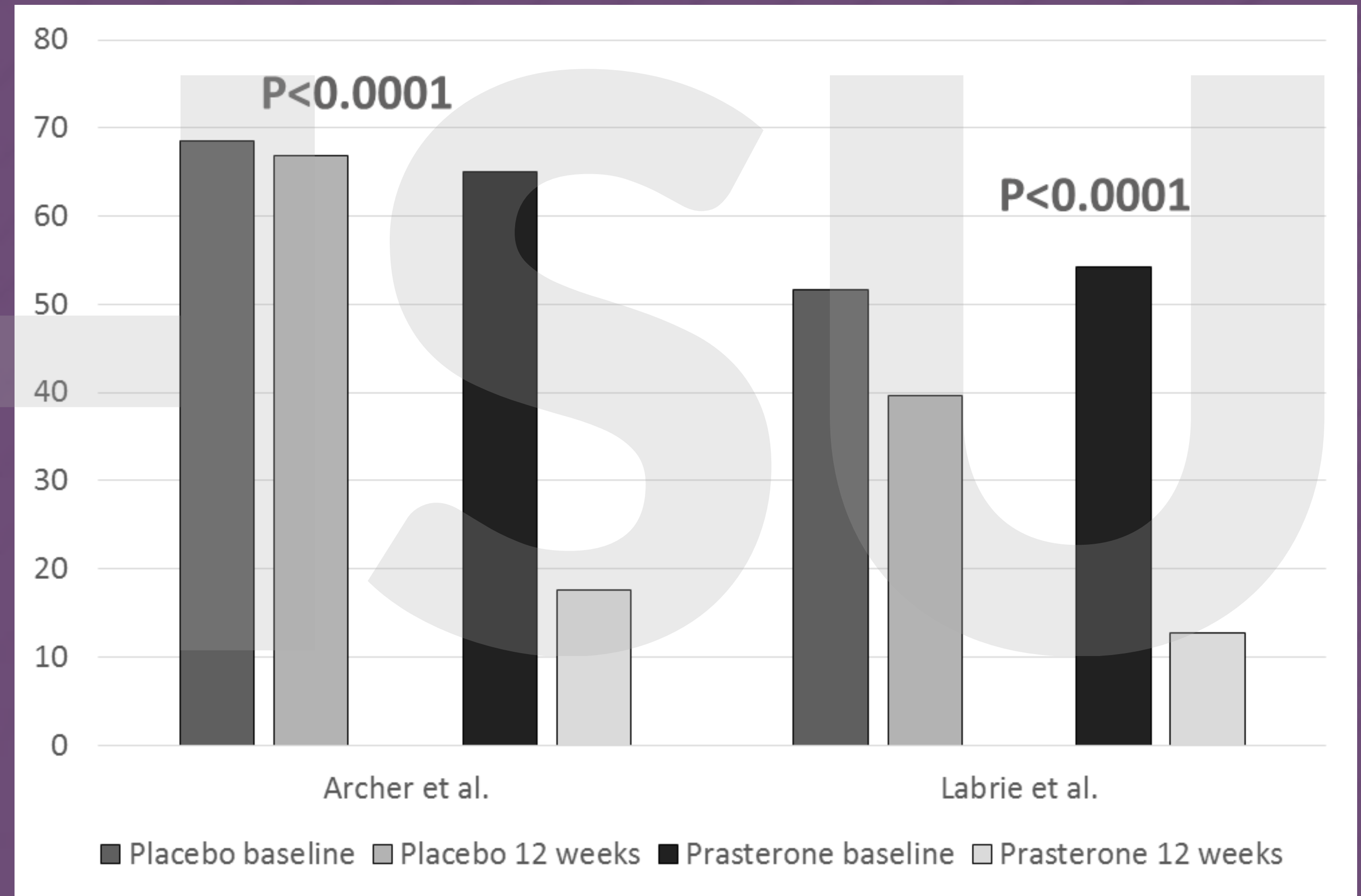
Difference from placebo: Prasterone (Week 12 mean – Baseline mean) – Placebo (Week 12 mean – Baseline mean). p-value calculation analysis of covariance using treatment as the main factor and baseline value as the co-variate



[1] Archer et al. Menopause 2015;22: 950-963.
[2] Labrie et al. Menopause 2016; 23: 243-256.

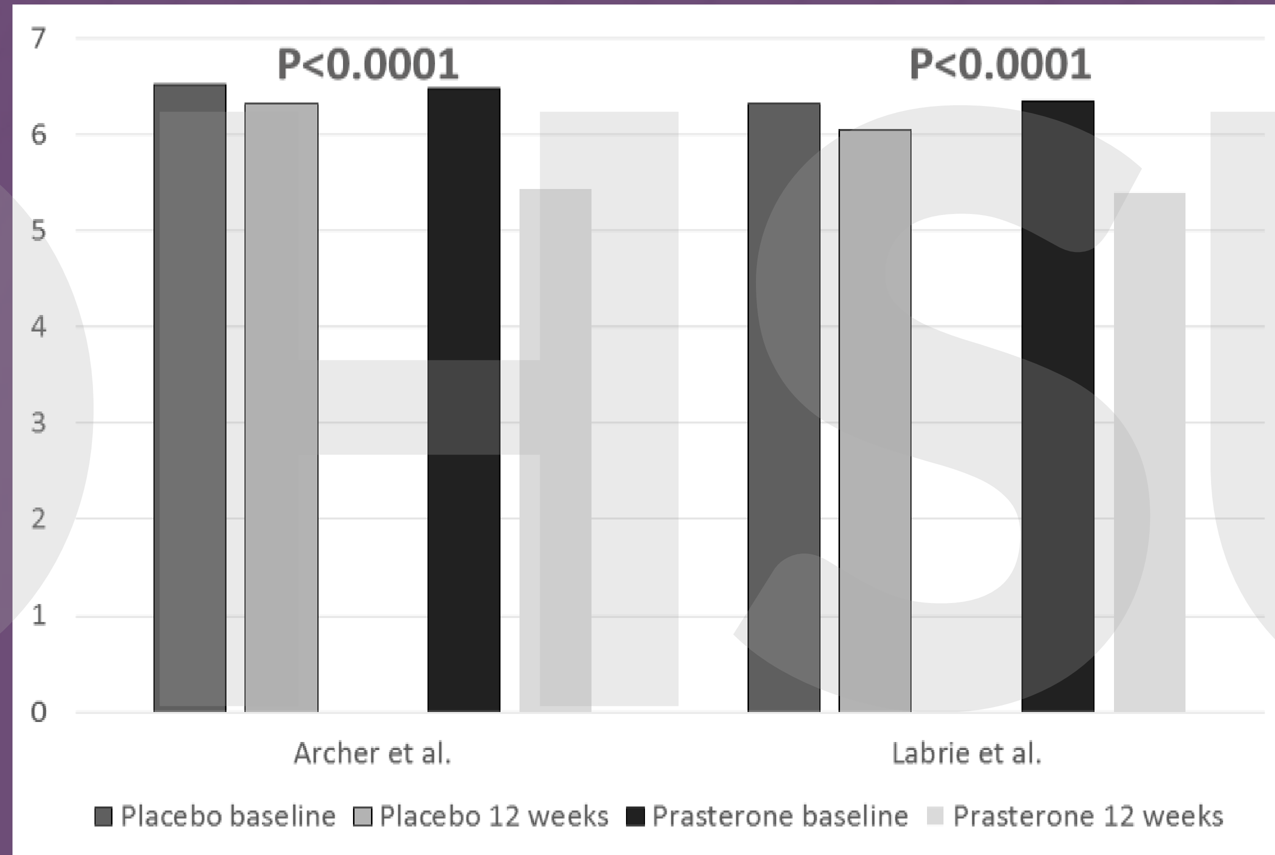
Significant Decreases in % Parabasal Cells with Prasterone Vaginal Inserts

Difference from placebo: Prasterone (Week 12 mean – Baseline mean) – Placebo (Week 12 mean – Baseline mean). p-value calculation analysis of covariance using treatment as the main factor and baseline value as the co-variate.



[1] Archer et al. Menopause 2015;22: 950-963.
[2] Labrie et al. Menopause 2016; 23: 243-256.

Significant Decreases in Vaginal pH with Prasterone Vaginal Inserts



[1] Archer et al. Menopause 2015;22: 950-963.
[2] Labrie et al. Menopause 2016; 23: 243-256.

Adverse Reactions

- 4 placebo-controlled, 12-week clinical trials (n=1,129), **vaginal discharge** was the most frequently reported adverse reaction (**5.71%** prasterone versus 3.66% in the placebo group)[1]
- In a 52-week non-comparative clinical trial (n=521), vaginal discharge was reported in 14.2% of women and **abnormal Pap smear in 2.1%**
  - 11 cases of abnormal Pap smear at 52 weeks included 1 case of low-grade squamous intraepithelial lesion (LSIL) and 10 cases of atypical cells of undetermined significance (ASCUS)
    - **5 HPV negative; 4 status unknown; 1 HPV positive[2]**

[1]INTRAROSA® Prescribing Information, AMAG Pharmaceuticals, February 2018.
[2]Data on File. ERC-230 Clinical Study Report. AMAG Pharmaceuticals 2017.

Provided as a courtesy by AMAG Pharmaceuticals, Inc. Please see full Prescribing Information.

Vaginal moisturizers: Research

- Replens has beneficial clinical effects
  - Symptomatic improvement
  - Clinical improvement
    - Dryness, pallor, mucosal thinning, petechiae and labial atrophy
- Vaginal cytology
  - Treatment with Replens increased mean cellular area, no change in maturation index
  - Replens lowers vaginal pH due to acidity and buffering capacity
  - Mean vaginal pH: **5.8-5.2 to 4.8-4.7** (12 weeks of therapy)

Bachmann GA. *Clin Pract Sex* 1991;7:1-8.
Fertil Steril 1994;61:178-80.

Hybrid Moisturizer/Lubricant

- **LUVENA**
- Prebiotics
- Lacto-peroxidase and lactoferrin
- Purportedly Inhibits candida and bacteria
- Works as both a moisturizer and a lubricant

Costantino D and Guaraldi C. *Minerva Ginecol* 2008;60(2):121-5.

Vulvar Soothing Creams—No Data

Neogyn vulvar soothing cream® (cutaneous lysate)

- >100 cytokines
- Growth factors
- Interferons and anti-inflammatory interleukins: IL-1RA, IL-4, and IL-10

**In clinical studies: improvement (vs placebo) in symptoms of vulvar pain and dyspareunia in vulvar pain patients*

Vajuvenate

- Avocado butter, coconut oil, sunflower oil

Releveum with 4%lidocaine (Desert Harvest)

Donders G. *J Lower Genital Tract Dis* 2012;16:

Vaginal Atrophy Treatment: Non-hormonal Therapy

Lubricants	Moisturizers
Temporarily moisten	Maintain hydration
	Can last for 2-3 days

Marshall DD, et al. *OBG Management.* 2009; Bachmann G, et al. *Up to Date.* 2012.

Non-hormonal Therapy: Lubricants

- Local solutions that temporarily moisturize the vaginal epithelium
- Must be applied at time of intercourse

Marshall DD, et al. *OBG Management.* 2009; Bachmann G, et al. *Up to Date.* 2012; www.amazon.com; www.drugstore.com.

Avoid: Oil- and Petroleum-based Lubricants, Warming Gels, Menthols

Marshall DD, et al. *OBG* Management. 2009.

Non-hormonal Therapy: Moisturizers

- Gels or creams used regularly to maintain hydration of the vaginal epithelium for long-term relief of vaginal dryness
- Effects last two to three days

Marshall DD, et al. *OBG Management.* 2009; Bachmann G, et al. *Up to Date.* 2012; Lee YK, et al. *Obstet Gynecol.* 2011; www.amazon.com; www.drugstore.com.

TABLE Lubricants and moisturizers for treating GSM and VVA*,[6,7]

Treatment	Comments	Available products
Lubricants		
Water-based	Ingredients: deionized water, glycerin, propylene glycol; latex safe; rare irritation; dry out with extended sexual activity	Astroglide, Good Clean Love, K-Y Jelly, Natural, Organic, Pink, Sliquid, Sylk, Yes
Oil-based	Ingredients: avocado, olive, peanut, corn; latex safe; can be used with silicone products; staining; safe (unless peanut allergy); nonirritating	Coconut oil, vegetable oil, vitamin E oil
Silicone-based	Ingredients: silicone polymers; staining; typically nonirritating; long lasting; waterproof; should not be used with silicone dilators, sexual toys, or gynecologic products	Astroglide X, Oceanus Ultra Pure, Pink Silicone, Pjur Eros, Replens Silky Smooth, Silicone Premium JO, SKYN, Überlube, Wet Premium
Petroleum-based	Staining; ingredients: mineral oil, petroleum jelly, baby oil; irritating; not latex safe and not for use with cervical caps or intravaginal diaphragms	Rarely recommended
Fertility friendly	Minimize harm to sperm motility; designed for couples trying to conceive	Astroglide TTC, Conceive Plus, Pre-Seed, Yes Baby

ObGManagement April 2017

Moisturizers		
Vaginal moisturizers	For maintenance use 1 to 3 times weekly; can benefit women with dryness, chafing with ADL, and recurrent vaginal infections irrespective of sexual activity timing	Balance Active Menopause Vaginal Moisturizing Lubricant, Canesintima Intimate Moisturizer, Replens, Rephresh, Sylk Natural Intimate Moisturizer, Yes Vaginal Moisturizer
Hybrids	Properties of both water- and silicone-based products (combination of a vaginal lubricant and moisturizer); nonirritating; good option for women with allergies and sensitivities	Lubrigyn, Luvena

*Before using or recommending a product patients and their providers should check a product's pH, ingredients, and additives, and ensure the product is 510K FDA cleared.

Abbreviations: ADL, activities of daily living; FDA, US Food and Drug Administration; GSM, genitourinary syndrome of menopause; VVA, vulvovaginal atrophy.

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Available Moisturizers

Product	Ingredients	Use	Price	Studies
Replens	Polycarbophil glycerin, mineral oil	Every 3 days	$17.5/14 app	Yes
LUVENA	Lactoperoxidase lactoferrin	2×/wk	$20/ 5 app	Yes
KY Liquibeads (ovules)	Dimethicone, gelatin, glycerin, dimethiconol	1-7d/wk		No
KY long lasting	Various polymers glycerin, mineral oil	2-3×/wk	$16/6 app	No
Emerita personal moisturizer	Aloe vera gel, calendula, vitamin E, ginseng, chamomile, allantoin	As needed	$16/4 oz	No
Moist again	Carbomer, aloe glycerin, chlorhexidine	As needed	$7/4 oz	No
Hyalofemme	Hyaluronic acid	7 days >2/wk	$17/30 gram	HA-yes
Pre-seed	Hydroxyethylcellulose, pluronic, arabinogalactan	As needed	$20/9 app	Yes

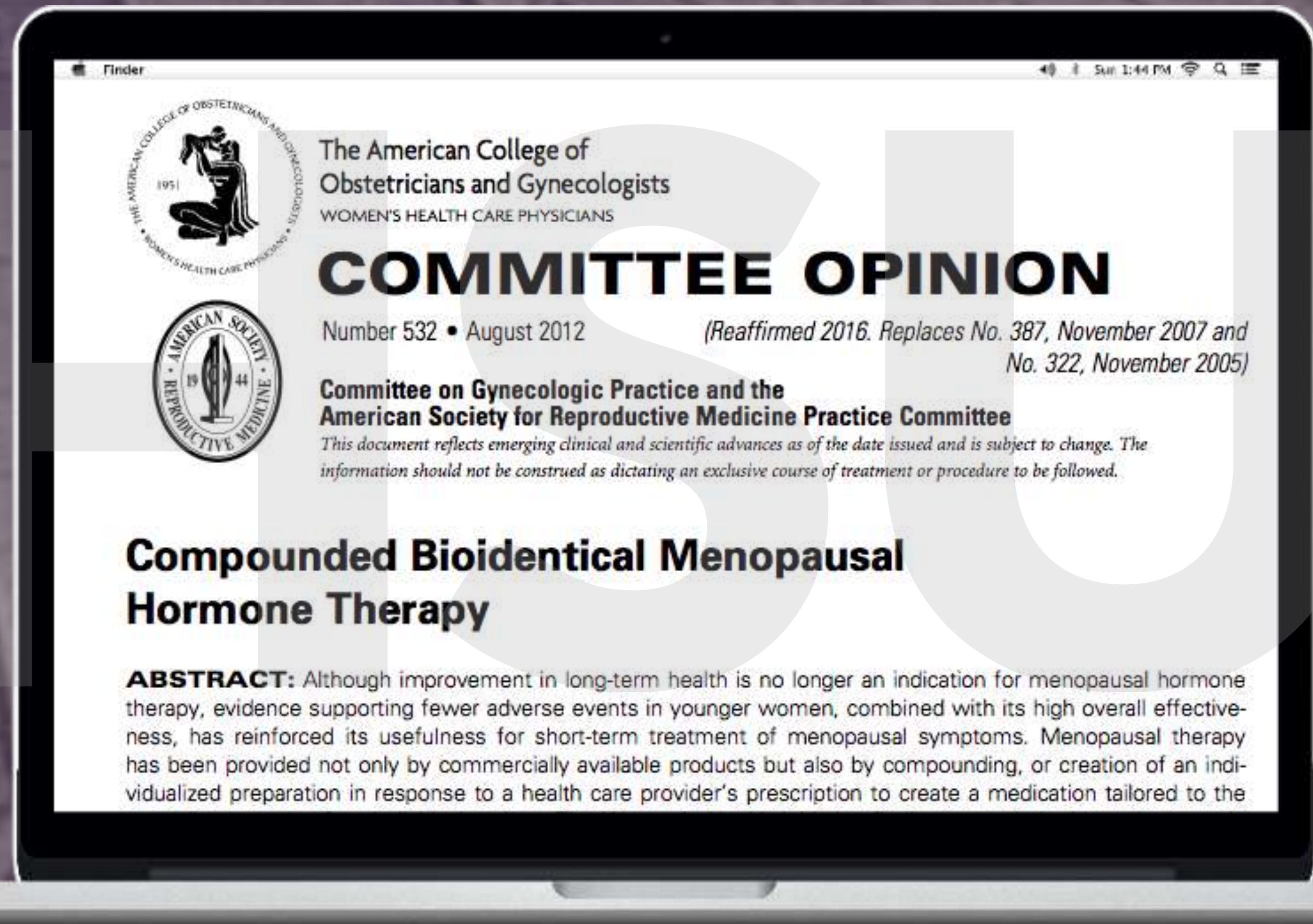
Not Effective, Not Recommended Therapies for Vaginal Atrophy

- Cooking oils
- Oral phytoestrogens
- Black cohosh
- Vaginal vitamin E
- Omega-3 supplements

Hill DA, et al. *Am Fam Physician.* 2010; Bachmann G, et al. *Up to Date.* 2012; Marshall DD, et al. *OBG Management.* 2009.

Bioidentical Hormones

No data to support they are safer than synthetic hormones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The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

COMMITTEE OPINION

Number 532 • August 2012 (Reaffirmed 2016. Replaces No. 387, November 2007 and No. 322, November 2005)

Committee on Gynecologic Practice and the American Society for Reproductive Medicine Practice Committee

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

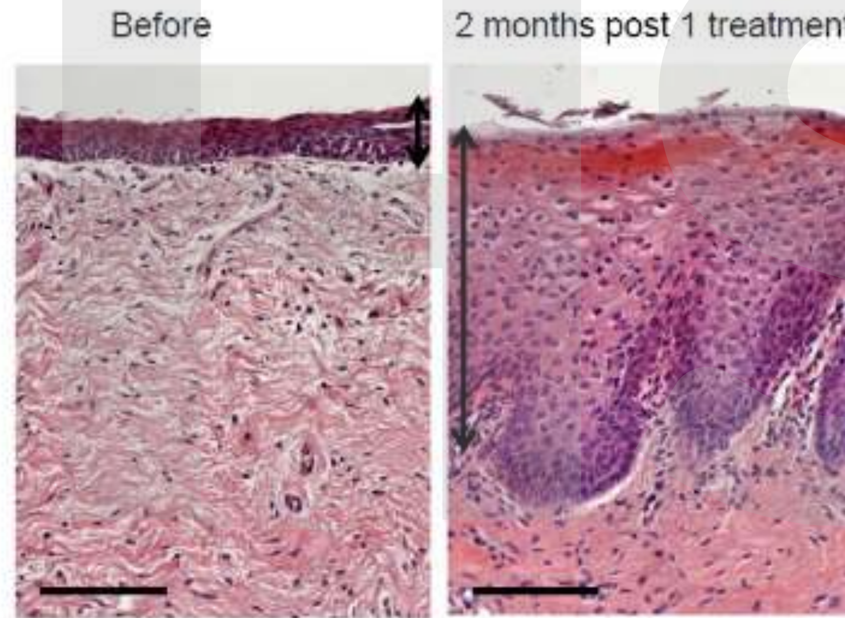
Compounded Bioidentical Menopausal Hormone Therapy

ABSTRACT: Although improvement in long-term health is no longer an indication for menopausal hormone therapy, evidence supporting fewer adverse events in younger women, combined with its high overall effectiveness, has reinforced its usefulness for short-term treatment of menopausal symptoms. Menopausal therapy has been provided not only by commercially available products but also by compounding, or creation of an individualized preparation in response to a health care provider's prescription to create a medication tailored to the

ACOG Committee on Gynecologic Practice. *Obstet Gynecol.* 2005; reaffirmed 2016.

Histologic Changes Fractional CO_2

Physiology in Gynecology



B&A images with the same enlargement

Scale bars: 100 μm

*Zerbinati N, et al. Microscopic and ultrastructural modifications of postmenopausal atrophic vaginal mucosa after fractional carbon dioxide laser treatment; Lasers Med Sci 2014 (pub. on-line)

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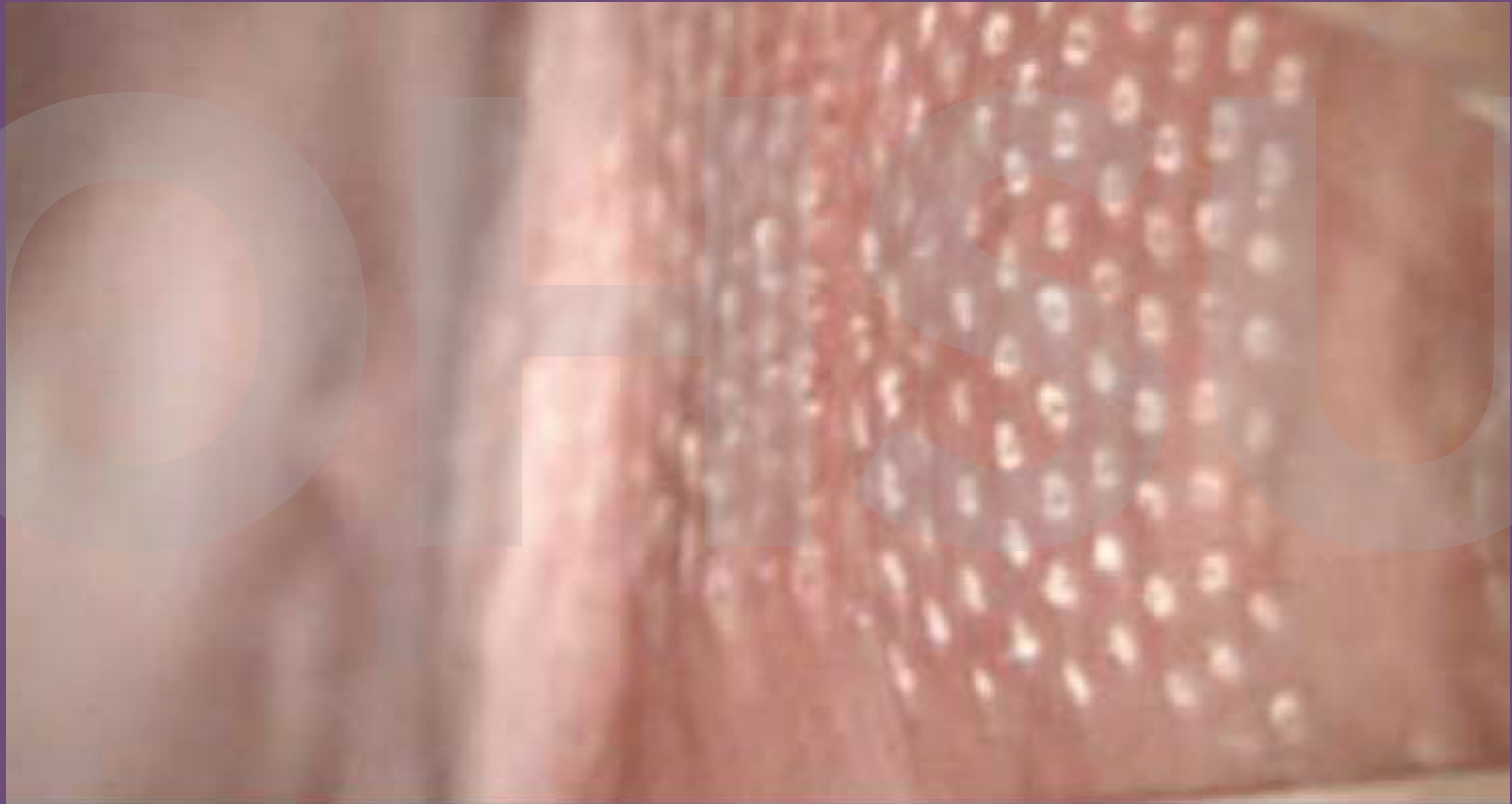
Fractionated CO_2



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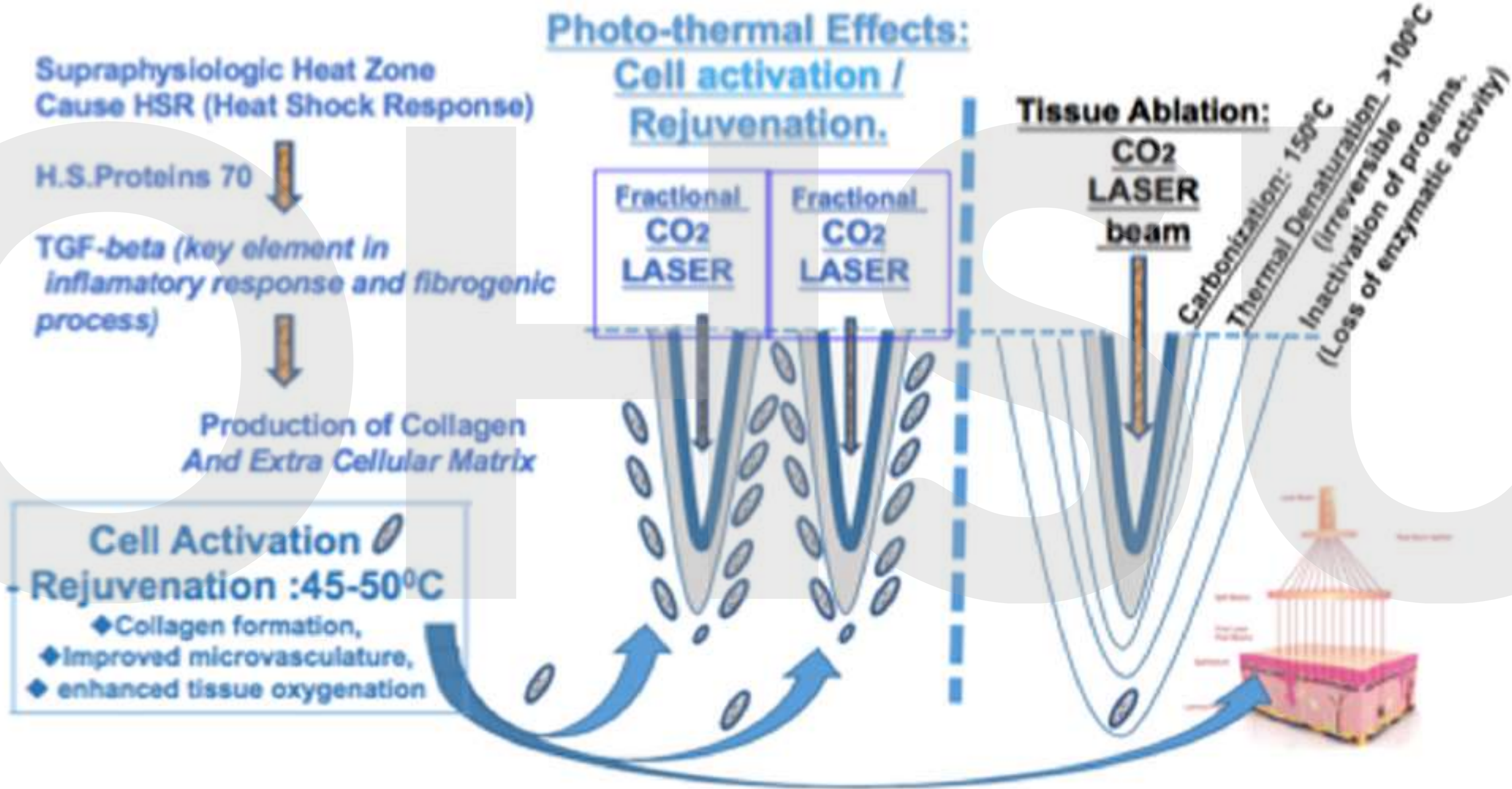

Fig. 6. (**A**) Fractional micro-ablation inducing cell activation and tissue rejuvenation at 45–50°C [42]. (**B**) Tissue ablation and thermal effects on adjacent layers (Courtesy: Tadir Y).

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Finder
Sun 1:44 PM
The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS
ACOG
THE AMERICAN CONGRESS
OF OBSTETRICIANS
AND GYNECOLOGISTS
Fractional Laser Treatment of
Vulvovaginal Atrophy and
U.S. Food and Drug Administration Clearance
Position Statement
The American College of Obstetricians and Gynecologists and
The American Congress of Obstetricians and Gynecologists
Several media outlets have described fractional carbon dioxide (CO2) laser as "approved" or "cleared" by the U.S. Food and Drug Administration (FDA) for the treatment of vulvovaginal atrophy (http://www.medicaldaily.com/fda-approves-mona-lisa-touch-laser-vaginal-dryness-caused-vaginal-atrophy-313184, http://www.realself.com/question/seattle-wa-the-monalisa-touch- and-work, and
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Ablative, Non-ablative, Fractional

Principles

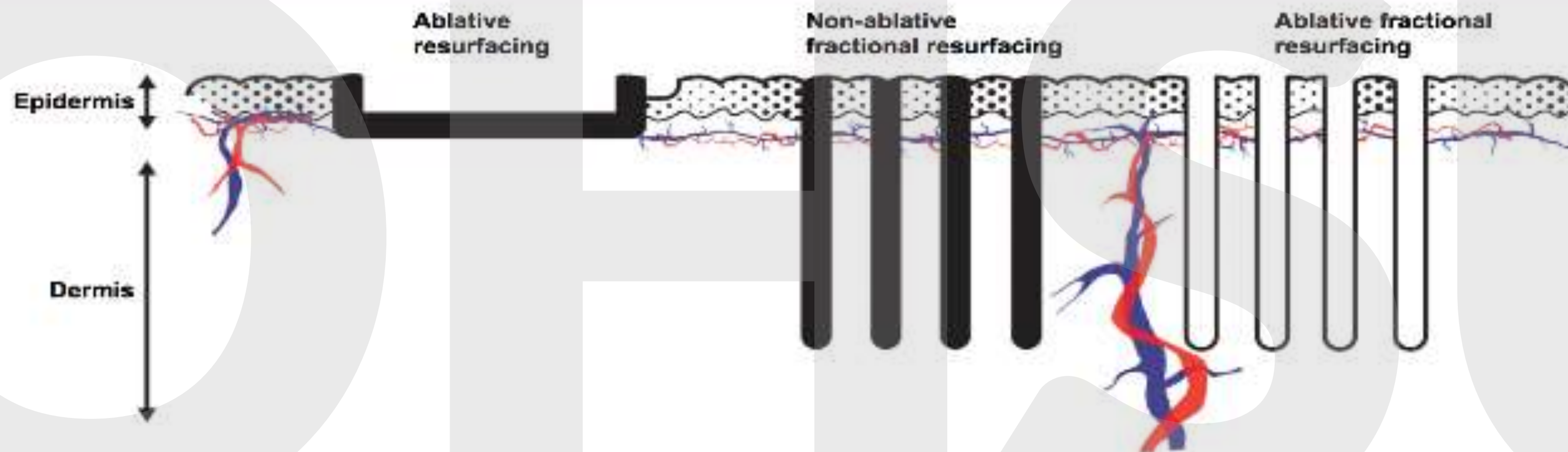

Figure 4 Ablative resurfacing (CO_2, erbium: yttrium aluminium garnet [Er:YAG]) versus non-ablative fractional resurfacing (erbium [Er:glass) versus ablative fractional resurfacing (CO_2, Er:YAG, Er: yttrium scandium gallium garnet [YSGG]).

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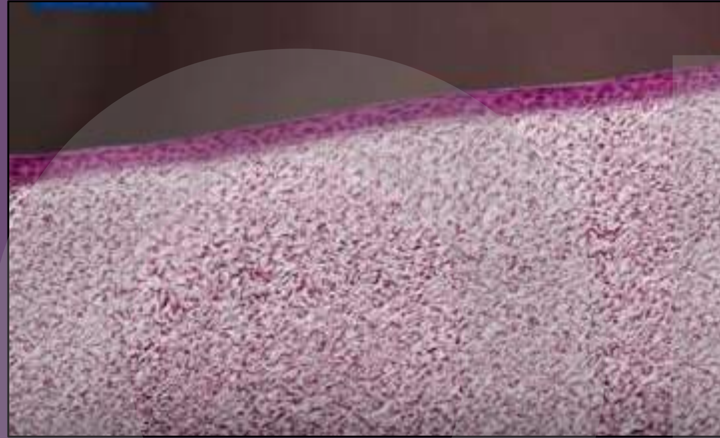
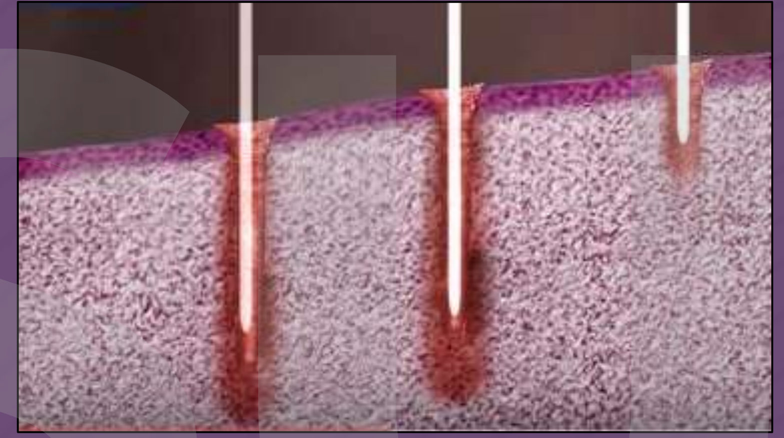
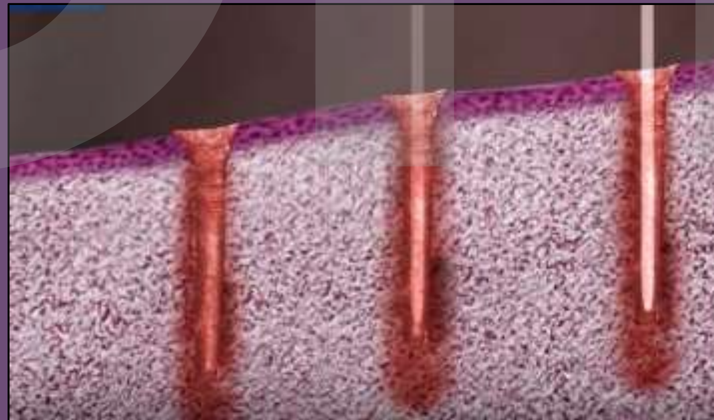
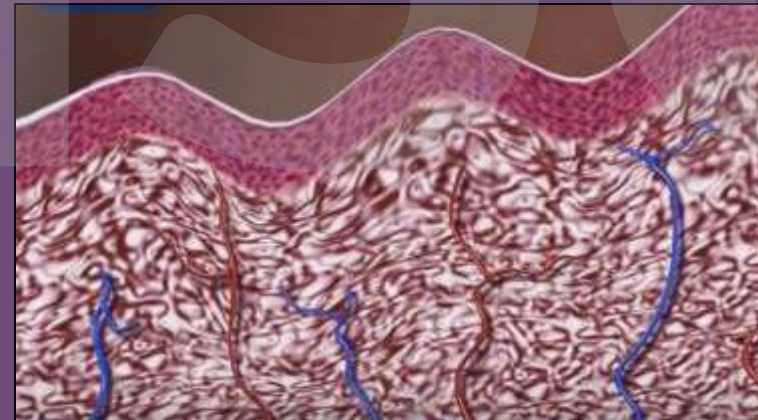
Fractional Photothermolysis: Mucosa









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FDA Clearance?

Incision, excision, ablation, vaporization and coagulation of body soft tissues in medical specialties, including aesthetic (dermatology & plastic surgery), podiatry, otolaryngology (ENT), **gynecology**, neurosurgery, orthopedics, geneal and thoracic surgery (including open and endoscopic), dental and oral surgery and genitourinary surgery.

FDA Notifications 30 July 2018

Venus Concept: **vaginal** health restoration

Cynosure: painful symptoms of **menopause and intimacy**, **penetrate vaginal wall** and stimulates cells

Alma: to improve vaginal irregularities, vaginal mucosa revitalization

Sciton DiVa: laser vaginal therapy

Thermiva: vaginal rejuvenation

InMode: Vaginal rejuvenation and urinary stress incontinence

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SGS 2018 Systematic Review Group SRG

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Fractional CO_2 Laser

Outcome	No. Studies	Total N	Methodological Quality	Other Considerations	Evidence Quality	Effect	Outcome Importance
Vaginal Maturation Indices	1	22	1A (0)	0	Moderate	Equal	Moderate
Vaginal health index	6	319	1A, 5C (0)	0	Low	Favors laser	Moderate
Dryness	7	311	1A, 6C (-1)	0	Low	Improved	Critical
Burning	5	200	1A, 4C (-1)	0	Low	Improved	High
Dyspareunia	9	369	1A, 8C (-1)	0	Low	Improved	Critical
Dysuria	3	127	3C (-1)	-1	Low	Improved	Moderate
ICIQ - SF	1	161	1C (0)	0	Low	Improved	High
FSFI	3	128	1A, 2C (0)	-1	Low	Equal	High
Pain during insertion	2	76	2C (-1)	0	Low	Minimal	Moderate

Erbium Laser vs Estrogen

Outcome	No. Studies	Total N	Methodological Quality	Other Considerations	Evidence Quality	Effect	Outcome Importance
Dryness	2	112	1B , 1C (-1)	-2	Low	Equal	Critical
Dyspareunia	2	112	1B, 1C (-1)	-2	Low	Equal	Critical
Irritation	1	50	1B (-1)	-1	Low	Favors laser	High
Vaginal health index	1	62	1B (0)	0	Moderate	Favors laser	Moderate
Maturation value	1	50	1C (0)	-1	Moderate	Favors laser	Moderate
Vaginal pH	1	50	1C (0)	-1	Moderate	Favors laser	Moderate
ICIQ-SF	1	19	1B (0)	0	Moderate	Improved	High

Balance of Benefits and Harms

Erbium laser is not superior to local estrogen for vaginal dryness and dyspareunia

There are minimal comparative data for fractional CO_2 laser

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Menopause: The Journal of The North American Menopause Society
Vol. 25, No. 1, pp. 21-28
DOI: 10.1097/GME.0000000000000955
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Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO_2 laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women

Vera L. Cruz, MD,[1] Marcelo L. Steiner, MD, PhD,[2] Luciano M. Pompei, MD, PhD,[2] Rodolfo Strufaldi, MD, PhD,[2] Fernando L. Afonso Fonseca, PhD,[3] Lucila H. Simardi Santiago, MD, PhD,[4] Tali Wajsfeld, MD,[1] and Cesar E. Fernandes, MD, PhD[1,2]

Abstract

Objective: The aim of the study was to evaluate efficacy of fractional CO_2 vaginal laser treatment (Laser, L) and compare it to local estrogen therapy (Estriol, E) and the combination of both treatments (Laser + Estriol, LE) in the treatment of vulvovaginal atrophy (VVA).

Methods: A total of 45 postmenopausal women meeting inclusion criteria were randomized in L, E, or LE groups. Assessments at baseline, 8 and 20 weeks, were conducted using Vaginal Health Index (VHI), Visual Analog Scale for VVA symptoms (dyspareunia, dryness, and burning), Female Sexual Function Index, and maturation value (MV) of Meisels.

Results: Forty-five women were included and 3 women were lost to follow-up. VHI average score was significantly higher at weeks 8 and 20 in all study arms. At week 20, the LE arm also showed incremental improvement of VHI score ($P = 0.01$). L and LE groups showed a significant improvement of dyspareunia, burning, and dryness, and the E arm only of dryness ($P < 0.001$). LE group presented significant improvement of total Female

TABLE Comparison of VAS and FSFI scores by treatment group in a randomized trial (45 participants) by Cruz and colleagues

VAS scores[a]				
	Laser	Estriol	Laser plus estriol	*P*[c]
Dyspareunia				
Baseline	4.9 (3.7)	3.2 (3.4)	6.5 (3.9)	.09
Week 20	0.7 (1.5)	0.2 (0.6)	0.9 (1.8)	.95
Dryness				
Baseline	8.0 (2.6)	5.6 (2.9)	7.9 (3.0)	.07
Week 20	1.4 (2.0)	0.5 (1.4)	0.3 (.07)	.35
Burning				
Baseline	3.9 (4.5)	0.9 (1.6)	4.9 (3.8)	.017[d]
Week 20	0.5 (1.5)	0.1 (0.3)	0.4 (1.1)	.95
Total FSFI scores[b]				
Baseline	18.6 [16.4; 24.6]	23.6 [17.5; 29.8]	18.7 [7.2; 22.6]	.21
Week 20	14.4 [7.8; 22.4]	25.4 [16.8; 29.3]	23.6 [14.9; 28.6]	.10

[a]Items listed as mean (SD).

[b]Items listed as median [interquartile range].

[c]P values of .05 were considered statistically significant.

[d]P<.05.

Abbreviations: FSFI, Female Sexual Function Index; VAS, visual analog scale.

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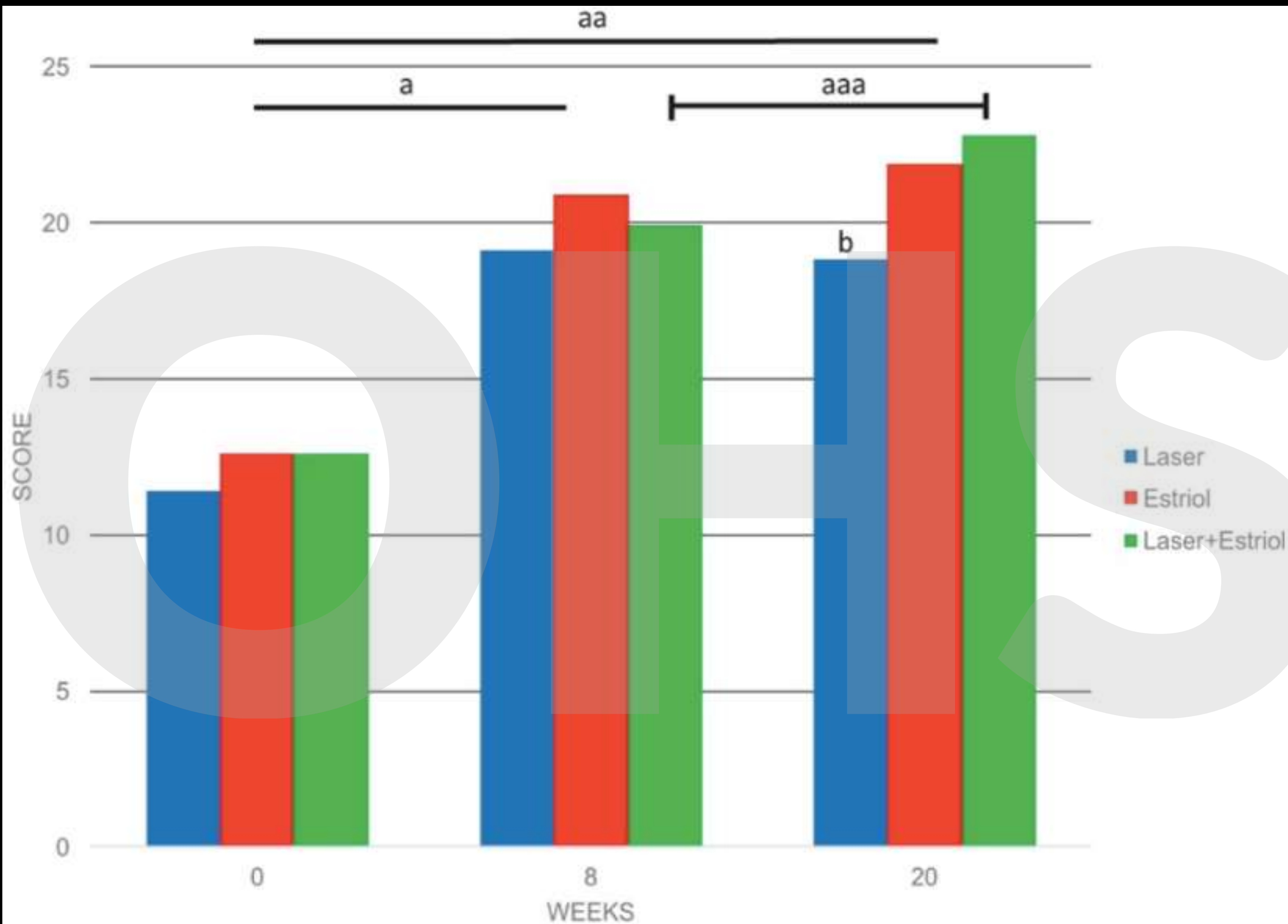

VHI score of different treatment arms at multiple time-points. aWilcoxon test $P<0.05$, all groups; aaWilcoxon test $P<0.001$, all groups; aaaWilcoxon test, LE week 8 vs week 20, $P=0.01$; bKruskal-Wallis test, L vs E and LE, $P<0.05$; Friedman test for multiple timepoints, $P<0.001$, all groups.

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The Vaginal Laser versus Vaginal Estrogen Therapy: The VeLVET Trial

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MFR Paraiso[1], CA Ferrando[1], M Karram[2], ER Sokol[3], CR Rardin[4], CA Matthews[5], CB Iglesia[6]

Sections of Urogynecology and Reconstructive Pelvic Surgery

[1]Cleveland Clinic Cleveland, OH; [2]Christ Hospital, Cincinnati, OH; [3]Stanford University Hospital, Palo Alto, CA; [4]Women and Infants Hospital, Providence, RI; [5]Wake Forest, Winston-Salem, NC; [6]Medstar Washingto

Washington DC

6 Month Outcome Data N=62

Outcome	Fractionated C02 laser N=33	Conjugated estrogen cream N=29	P value
Mean difference VAS score Dryness Itching Irritation Dysuria	 -5.48 ± 2.68 -1.84 ± 3.01 -3.29 ± 3.73 -1.4 ± 2.89	 -5.76 ± 2.48 -1.24 ± 2.96 -3.49 ± 3.19 -2.11 ± 2.85	 0.67 0.45 0.87 0.36
Mean difference VHI	0.9 ± 0.7	1.2 ± 0.9	0.07
Mean difference DIVA	-3.3 ± 3.2	-4.4 ± 3.1	0.18
Mean difference VMI^	3.9 ± 30.6	25 ± 22.6	0.04*
Mean difference FSFI	1.7 ± 6.7	4.9 ± 8.3	0.1
Mean difference UDI	-9.4 ± 15.7	-6.2 ± 12	0.37
% sexually active	45.5 (15)	48.3 (14)	0.82

*statistically significant at P ≤ 0.05
^remained statistically significant after controlling for confounding factors

6 Month FSFI Outcome Data N=62

	Fractionated C02 laser N=33	Conjugated estrogen cream N=29	p value
Mean difference FSFI Score1 Desire†	0.32±1.3	1.02±1.4	0.05*
Mean difference FSFI Score2 Arousal†	0.62±1.6	1.63±1.9	0.03*
Mean difference FSFI Score3 Lubrication	0.11±1.2	0.35±1.4	0.50
Mean difference FSFI Score4 Orgasm	0.37±1.3	0.9±1.6	0.17
Mean difference FSFI Score5 Satisfaction	0.88±2.1	1.7±1.7	0.50
Mean difference FSFI Score6 Pain	-0.59±2.8	-0.04±3.3	0.81

*statistically significant at $P \leq 0.05$
^remained statistically significant after controlling for confounding factors
†no longer statistically significant after controlling for confounding factors

Results: Adverse Events

- 10 adverse events (AE) mild or moderate: vaginal bleeding, pain, breast tenderness, UTI, migraine, and abdominal cramping
- AEs did not differ between groups

VELVET TRIAL Conclusion

- At 6-months, fractionated Co2 vaginal laser and vaginal estrogen treatment resulted in similar improvement in GSM symptoms but lower FSFI arousal and desire scores in the laser arm
- Similar patient satisfaction in both groups
- No serious adverse events

FINAL SUMMARY

1. First line GSM

   Moisturizers, lubricants

   Pelvic PT, dilators

2. Vaginal Exercise-—with or without a partner
3. Local hormone therapy for those who failed non-hormonal tx
4. Ospemifene oral tablet
5. DHEAS
6. Involve treating oncologist for breast cancer pts
7. Compounded off-label testosterone/estriol not recommended

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FINAL SUMMARY (continued)

8. Advertising Energy Based Therapy (EBT) for specific gynecologic conditions is PREMATURE
9. Early data suggests benefit for GSM but do need to discuss alternatives
10. Large scale comparative and sham trials needed

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Alliance for Advancing Women's Health

www.advancingwomenshealth.org

Finder

Sun 1:44 PM

EVENTS & ANNOUNCEMENTS

RESOURCES ABOUT THE ALLIANCE CONTACT US

Improving Women's Sexual Health Outcomes

Sexual health is an integral part of overall health and wellbeing, and can help improve social and emotional health.

But far too often women's sexual health concerns are not addressed, leaving women to suffer in silence. Making sure women of all ages and backgrounds have their concerns heard without feeling judged or ashamed is critical to improving their health and quality of life.

“Attention is the most basic form of love.”

Zen teacher John Tarrant

Thank you for your attention!

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