The WISDOM survey: Physicians' Level of Comfort Prescribing Treatment for Vulvar and Vaginal Atrophy (VVA) Symptoms in Women with a Predisposition or History of Breast Cancer

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Disclosures

- **Advisory board:** AMAG Pharmaceuticals, Palatin Technologies and Valeant Pharmaceuticals
- **Speaker's bureau:** Valeant Pharmaceuticals

VVA in Breast Cancer Survivors

- More than 60% of postmenopausal breast cancer patients experience symptoms of VVA including vaginal dryness and dyspareunia[1,2]
- VVA symptoms are the most poorly addressed side effects of adjuvant endocrine therapy including aromatase inhibitors[3]
- Local estrogen therapy is an approved treatment of VVA in menopausal women
- A major concern of prescribing vaginal estrogens in breast cancer survivors is the potential risk of systemic absorption and potential breast effects[3]

VVA: vulvar and vaginal atrophy.

1. Mac Bride MB, et al. *Mayo Clin Proc* 2010;85:87-94. **2.** Crandall, et al. *Menopause* 2004;11:519-530. **3.** NAMS. *Menopause* 2013;20:888-902.

Local Estrogen Therapy for Breast Cancer Survivors with VVA

- Local or systemic menopausal estrogen therapies for treating VVA are currently contraindicated for women with known, suspected, or a history of breast cancer
- Pharmacokinetic studies have found very low to non-existent systemic absorption of some low-dose, local, vaginal estrogen therapies[1-4]
- NAMS, ACOG, and IMS support using vaginal estrogens in women with a history of estrogen-dependent breast cancer who are unresponsive to non-hormonal therapies[5-7]

ACOG: American Congress of Obstetricians and Gynecologists; IMS: International Menopause Society; NAMS: North American Menopause Society.

1. Bachmann G, et al. *Obstet Gynecol.* 2008;111:67-76. **2.** Dorr MB, et al. *Fertil Steril.* 2010;94:2365-2368. **3.** Pickar JH, et al. *Climacteric.* 2016;19:181-187. **4.** Archer DF, et al. *Menopause.* 2017;24:510-516. **5.** NAMS. *Menopause.* 2013;20:888-902. **6.** ACOG. *Obstet Gynecol.* 2016;127:e93-96. **7.** de Villiers TJ, et al. *Climacteric*. 2016;19:313-315.

Estradiol Parameters for Vaginal vs Oral Estrogens

Route	Products	Dose	Sampling Time (d)	AUC_{0-24} (pg*h/mL)	C_{avg} (pg/mL)	C_{max} (pg/mL)
Vaginal	Premarin® Cream	0.3 mg CEE[1] 0.625 mg CEE[2]	7 7	231 ± 285 369 ± 28	9.6 15.4	12.8 ± 16.6 26.4
	Vagifem®[3]	10 µg estradiol 25 µg estradiol	14	157 439	6.6 18.3	15.8 35.8
	TX-004HR[4]	4 µg estradiol 10 µg estradiol 25 µg estradiol	14	87 ± 43 110 ± 55 172 ± 80	3.6 ± 1.8 4.6 ± 2.3 7.1 ± 3.3	4.8 ± 2.3 7.3 ± 2.4 15.7 ± 7.6
	Placebo[4]		**14**	**104 ± 66**	**4.3 ± 2.8**	**5.5 ± 3.4**
Oral	Estrace®[5]	2.0 mg estradiol	11	2642 ± 1156	110 ± 50	
	Premarin®[6]	0.3 mg CEE	7	325 ± 499	13.5	19.4 ± 24.7

Data expressed as mean ± SD, when possible.

CEE: conjugated equine estrogens

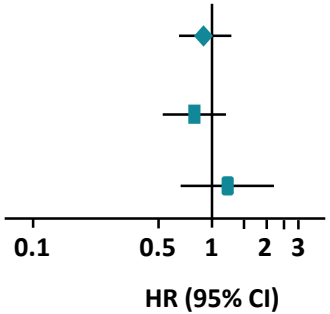
1. Premarin vaginal cream prescribing information. Wyeth Pharmaceuticals. **2.** Labrie F, et al. *Menopause.* 2009;16:30-36. **3.** Eugster-Hausmann M, et al. *Climacteric. 2010;13:219-227.* **4.** Archer DF, et al. *Menopause.* 2017;24:510-516. **5.** Scott RT, et al. *Obstet Gynecol.* 1991;77:758-764. **6.** Dorr MB, et al. *Fertil Steril.* 2010;94:2365-2368.

Breast Cancer Risk With Vaginal Estrogens

- In the WHI-Observational Study (1993-2005), the risk of invasive breast cancer in women with or without an intact uterus was not significantly different between vaginal estrogen users and nonusers

Breast cancer	n	VE use N events (rate*)	No VE use N events (rate*)	HR (95% CI)
Overall	45,663	40 (3.6)	1185 (4.1)	0.91 (0.64–1.29)
Intact uterus†	32,433	26 (3.2)	858 (4.0)	0.79 (0.51–1.22)
Hysterectomy†	14,133	14 (4.7)	327 (4.2)	1.23 (0.68–2.21)

*Rate/1000 person-year; †Numbers don't add up, due to the time varying nature of hysterectomy status: 903 change from no hysterectomy to hysterectomy and are counted in both cells.
CI: confidence interval; HR: hazard ratio; VE: vaginal estrogens.



Objective

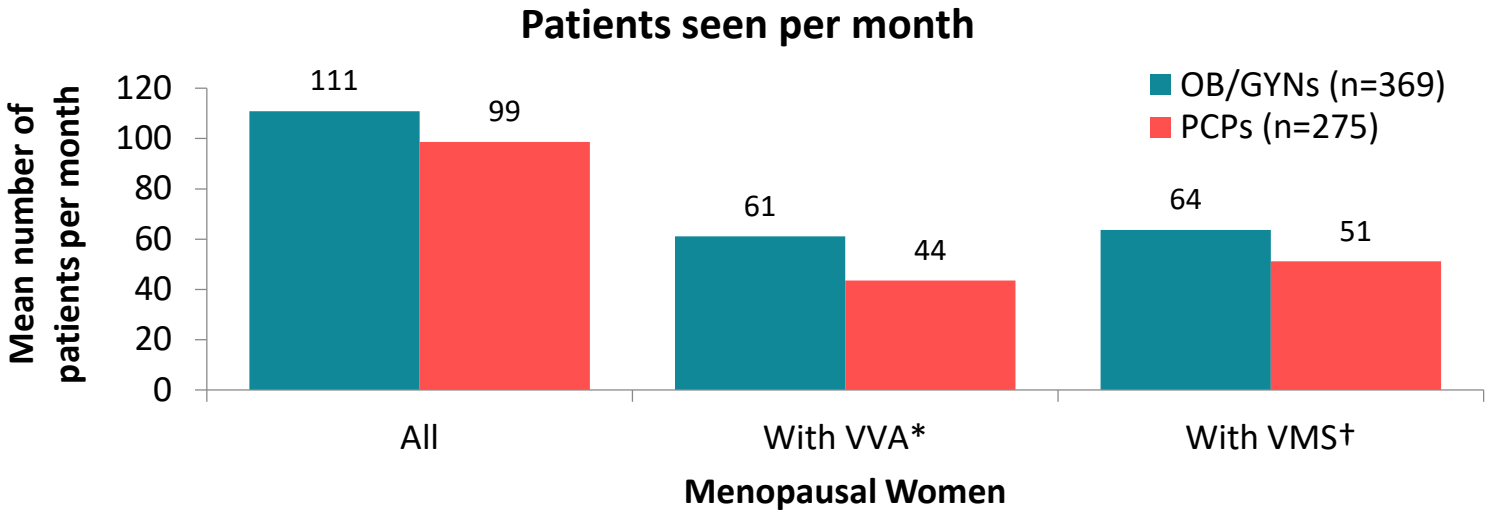
- To evaluate physicians' behaviors and attitudes regarding VVA treatment in menopausal women
  - The WISDOM survey
  - This report focuses on treating women with or without a history of breast cancer

Survey Topics

- Number of patients seen in a month, stratified by age
- Number of menopausal women with VVA or VMS symptoms
- Treatments used for VVA
- Beliefs on local estrogen therapy use
- Use of vaginal estrogen in women with breast cancer history or predisposition

Overview of Patients

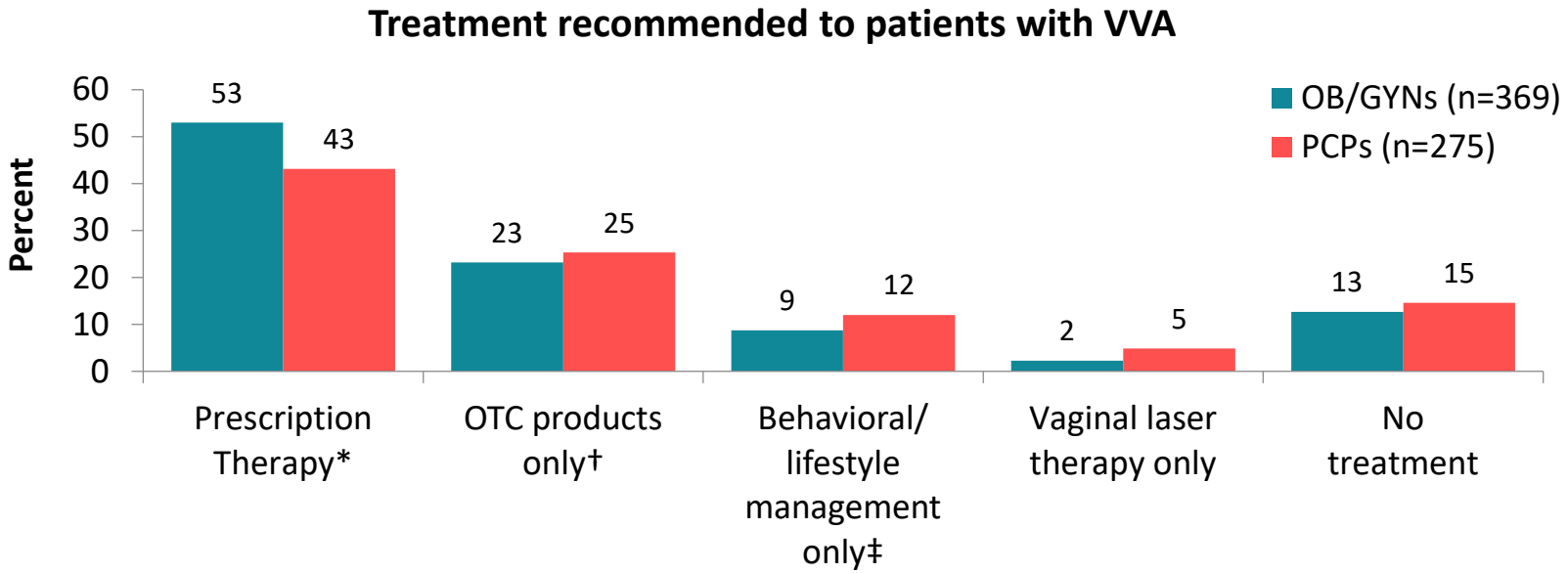
- In a typical month, OB/GYNs and PCPs see 111 and 99 menopausal women, respectively
  - Of these, 61 (55%) and 44 (44%) had VVA symptoms, respectively



*VVA symptoms such as painful intercourse (dyspareunia), vaginal dryness, vaginal itching and burning and/or bleeding with intercourse.
†VMS symptoms such as hot flashes and/or night sweats.

Treatments for VVA

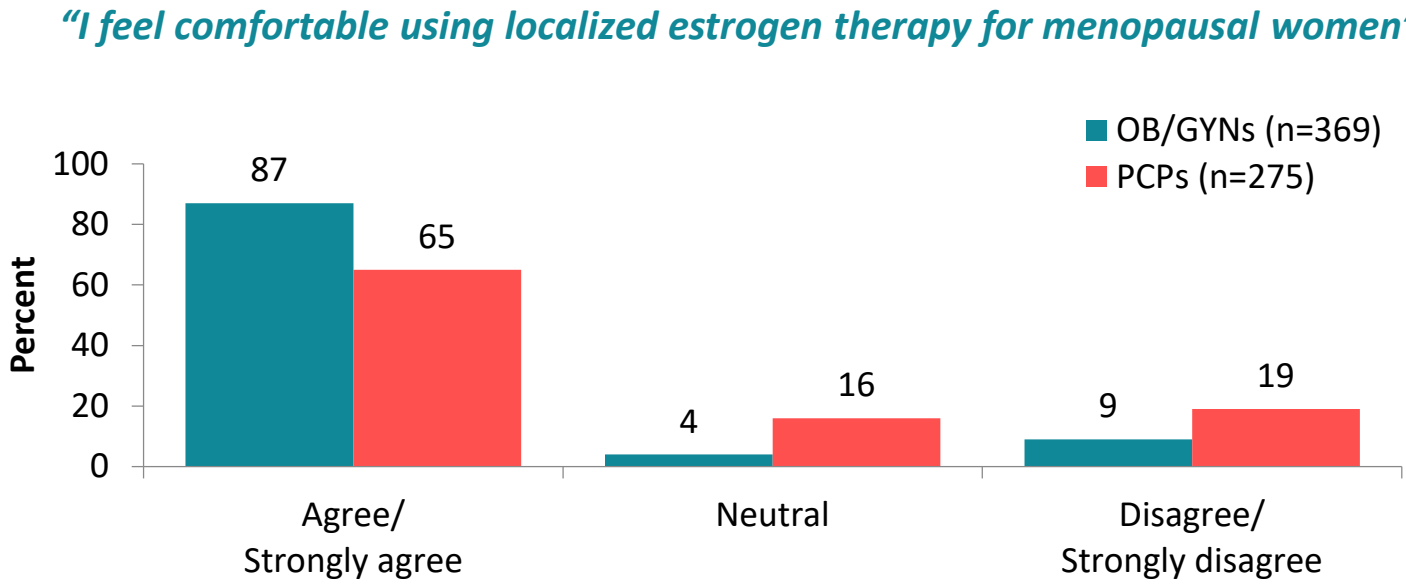
- Prescription therapy was the most common VVA treatment
  - More OB/GYNs than PCPS preferred to treat VVA with prescription therapy
  - OB/GYNs wrote more scripts per month than PCPs (44 vs 35)



*With or without any other type of treatment; †Vaginal lubricants and moisturizers; ‡Increased sex, vaginal dilation, other.
OTC: Over the counter.

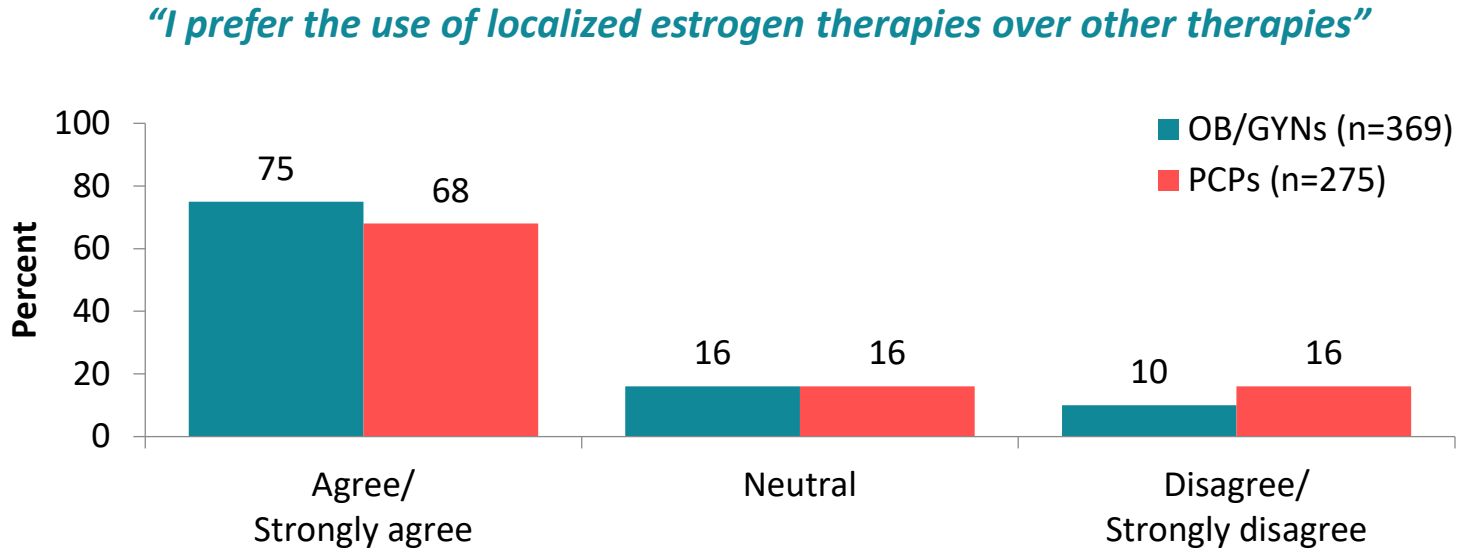
Local Vaginal Estrogen Use

- Most felt comfortable using localized estrogen therapy for menopausal women



Local Vaginal Estrogen vs Other Therapies

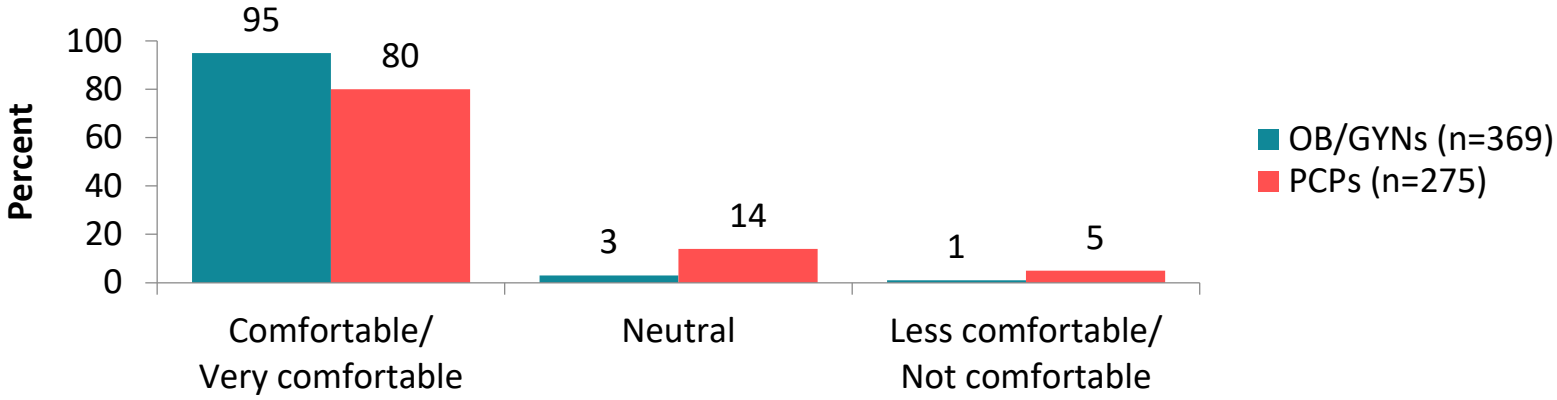
- Most physicians prefer using localized estrogen therapy over other therapies



No Personal History of Breast Cancer

- Most physicians were comfortable prescribing therapy to treat VVA among women with no personal history or predisposition to breast cancer

"How comfortable are you in using existing prescription therapy* to treat VVA in women with no personal history or predisposition to breast cancer"

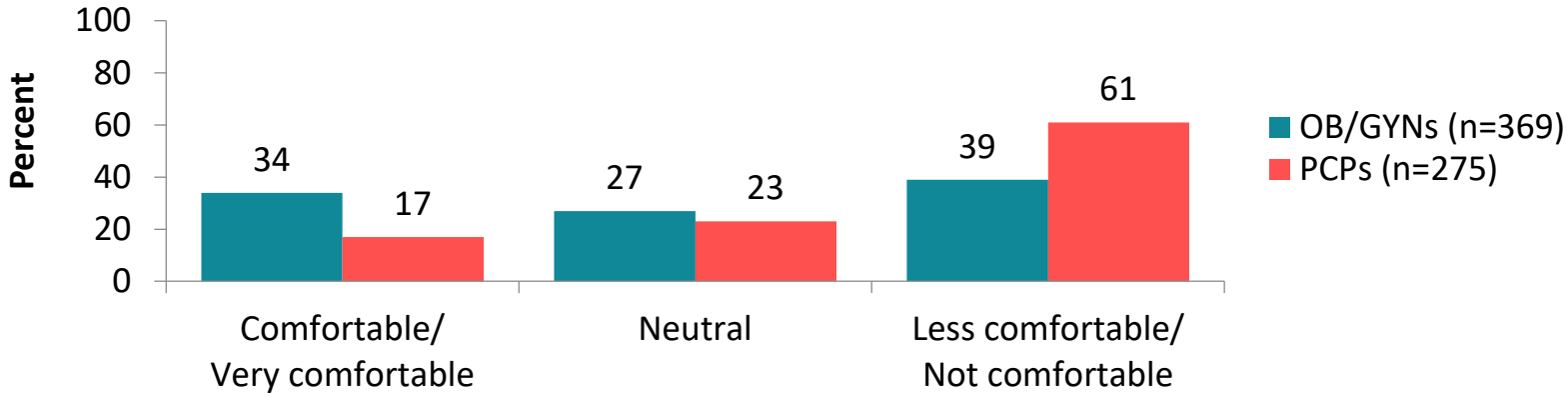


*Vaginal or oral ET, Osphena, Estring, DHEA, or other existing VVA products.

Personal History of Breast Cancer

- OB/GYNs seem to be more comfortable than PCPs prescribing existing therapy to women with a personal history of breast cancer
  - But only 34% of OB/GYNs are comfortable doing so

"How comfortable are you in using existing prescription therapy* to treat VVA in women with a personal history of breast cancer"

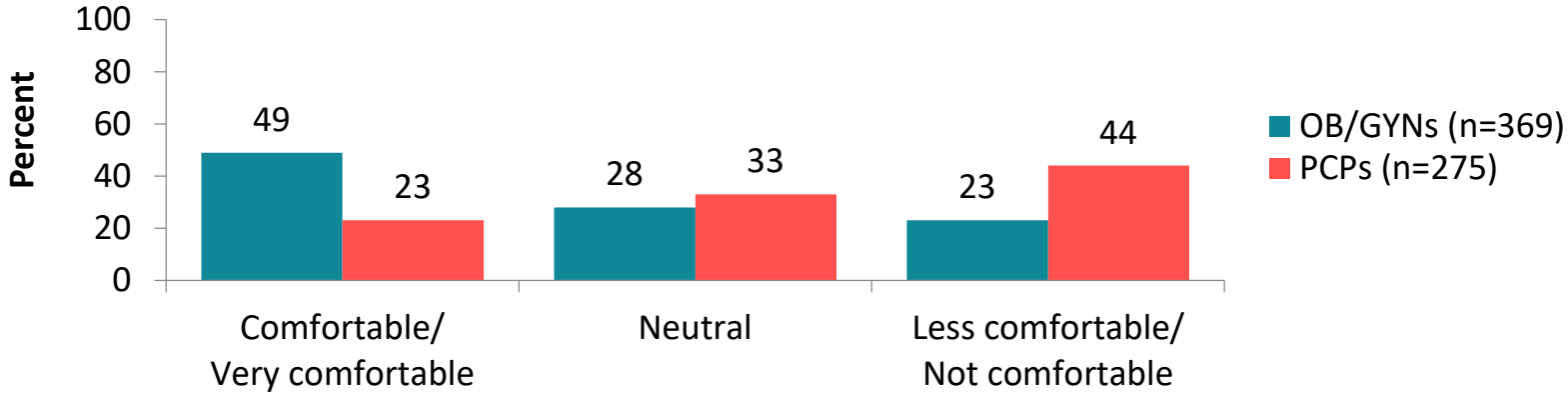


*Vaginal or oral ET, Osphena, Estring, DHEA, or other existing VVA products.

Predisposition to Breast Cancer

- OB/GYNs are more comfortable than PCPs prescribing therapy to women with a predisposition to breast cancer, such as a family history or a BRCA mutation
  - But only 49% of OB/GYNs are comfortable doing so

"How comfortable are you in using existing prescription therapy* to treat VVA in women with a predisposition to breast cancer†"



***Vaginal or oral ET, Osphena, Estring, DHEA, or other existing VVA products.**
†Family history, BRCA mutations, etc.

Conclusions

- Most OB/GYNs and PCPs are comfortable prescribing vaginal estrogen therapy for VVA, and prefer it over other products
- However, a relatively low percentage of OB/GYNs and PCPs are comfortable prescribing VVA therapies to women with a history of or a predisposition to breast cancer
    - Twice as many OB/GYNs felt comfortable prescribing therapy to women with a personal history or a predisposition to breast cancer than PCPs
- Physician comfort level is low despite
    - Medical-society support for using vaginal estrogen therapy in women with a history of estrogen-dependent breast cancer who were unresponsive to non-hormonal therapies[1-3]
    - Studies showing very low to negligible systemic absorption of estradiol with some vaginal products[4-7]

1. ACOG. *Obstet Gynecol.* 2016;127:e93-96. **2.** NAMS. *Menopause.* 2013;20:888-902. **3.** de Villiers TJ, et al. *Climacteric*. 2016;19:313-315. **4.** Bachmann G, et al. *Obstet Gynecol.* 2008;111:67-76. **5.** Dorr MB, et al. *Fertil Steril.* 2010;94:2365-2368. **6.** Pickar JH, et al. *Climacteric.* 2016;19:181-187. **7.** Archer DF, et al. *Menopause.* 2017;24:510-516.