

# WISDOM survey: attitudes and behaviors of physicians toward vulvar and vaginal atrophy (VVA) treatment in women including those with breast cancer history

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## Abstract

**Objective:** To evaluate and compare physicians' behaviors and attitudes regarding vulvar and vaginal atrophy (VVA) treatment in menopausal women, including women with breast cancer, using an internet-based survey.

**Methods:** The WISDOM survey queried obstetricians and gynecologists (OB/GYNs) and primary care physicians (PCPs) with 23 multipart questions assessing behaviors and attitudes towards VVA treatment.

**Results:** Of 2,424 surveys sent, 945 (39%) responded and 644 (27%) were completed. Of the menopausal women seen by OB/GYNs and PCPs, 44% to 55% reported having VVA symptoms. Physicians prescribed VVA treatments primarily because of effectiveness. Only 34% of OB/GYNs and 17% of PCPs felt comfortable prescribing VVA therapies to women with a personal history of breast cancer. In general, the most common VVA treatment recommended by all was prescription therapy (49%; with or without other therapies) in the form of US Food and Drug Administration-approved vaginal estrogen creams. More OB/GYNs (72%) than PCPs (47%) disagreed that VVA was best treated with over the counter than prescription products. Out-of-pocket cost and fear of risks associated with estrogens were believed to be the main barriers for why women choose not to get treated and why they discontinue treatment.

**Conclusions:** More OB/GYNs than PCPs prescribed VVA treatment, especially vaginal estrogens, for menopausal women, but both groups generally had similar attitudes and behaviors regarding VVA treatment. Physician comfort was low when prescribing to women with a history of breast cancer, despite women's health medical societies supporting vaginal estrogen use in women with a history of estrogen-dependent breast cancer who were unresponsive to nonhormonal therapies when offered in consultation with their oncologist.

**Key Words:** Attitudes – Menopause – Survey – Vaginal estrogen therapy – Vulvar and vaginal atrophy (VVA).

In the United States, 41.7 million women were reaching or were currently of menopausal age in 2010.<sup>1</sup> Menopausal symptoms are common, affecting up to 75% of menopausal women, and can negatively impact women's quality of life, personal and intimate relationships, and productivity.<sup>2,3</sup> Of the women afflicted with menopausal

symptoms, up to 45% experience symptoms of vulvar and vaginal atrophy (VVA), such as vaginal dryness, irritation, itching, dysuria, and pain or bleeding with sexual activity.<sup>4,5</sup> VVA, a component of the genitourinary syndrome of menopause (GSM),<sup>6</sup> can be progressive and may not resolve without treatment.<sup>7</sup>

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Breast cancer is the most common cancer in US women with an estimated 250,000 women diagnosed in 2017.<sup>8</sup> Most diagnoses of breast cancer are in postmenopausal women, with a median age of 62 years at diagnosis,<sup>8</sup> and are hormone receptor-positive breast tumors.<sup>9</sup> More than 60% of postmenopausal breast cancer patients report symptoms of VVA, notably vaginal dryness and dyspareunia.<sup>10,11</sup> These VVA symptoms are often the most poorly addressed side-effects of women on adjuvant endocrine therapy (e.g. Aromatase inhibitors).<sup>7</sup> Aromatase inhibitors, a standard treatment for many postmenopausal breast cancer patients, reduce breast cancer recurrence by inducing a profound estrogen-deficiency state prevented by the conversion of androgens to estrogens.<sup>7</sup> Such a low estrogen state can lead to VVA due to a lack of estrogen in the vaginal tissues.<sup>7,12,13</sup>

Vulvar and vaginal atrophy symptoms can be managed successfully with over-the-counter (OTC) products or US Food and Drug Administration (FDA)-approved prescription therapies, such as local estrogen therapy (ET).<sup>7</sup> In women with a history of estrogen-dependent breast cancer who are experiencing significant VVA, the American College of Obstetricians and Gynecologists (ACOG), The North American Menopause Society (NAMS), and the International Menopause Society (IMS) recommend the short-term use of vaginal low-dose ET in those who are unresponsive to lubricants and moisturizers, a recommendation which should be made in coordination with their oncologist.<sup>7,14,15</sup>

In the past decade, many international, large-scale surveys have been aimed towards understanding the attitudes of menopausal women regarding hormone therapy (HT) use,<sup>5,16-20</sup> whereas few physicians have been surveyed.<sup>21-25</sup>

The aim of the WISDOM survey was to evaluate and compare physicians' behaviors and attitudes regarding VVA treatment in menopausal women, with a focus on women with an elevated risk or personal history of breast cancer.

**METHODS**

**Survey conduct and design**

Rose Research, a market research firm, conducted an Internet survey assessing physicians' behaviors and attitudes towards VVA treatment. TherapeuticsMD, a pharmaceutical company focused on research and development of products exclusively for women's health, commissioned the survey. The project was managed entirely by Rose Research, which included questionnaire design, data tabulations, and analysis; Global Market Insite (GMI) was contracted to obtain a nationally representative sample of US physicians. GMI is an institutional review board-approved panel source, is a member of ESOMAR (the World Association for Opinion and Marketing Research), and complies with the International Chamber of Commerce/ESOMAR International Code on Market and Social Research. GMI's Global Panels are recruited and managed expressly for the purpose of conducting marketing research.

The WISDOM survey contained 23 multipart questions (17 are reported here) on the number and types of patients seen in a month, treatments used for VVA, types of prescriptions recommended, reasons why products were prescribed, barriers to prescription therapy, reasons for prescription therapy discontinuation, beliefs about local ET use, and use of vaginal estrogen in women with a predisposition or history of breast cancer (Table 1). This survey focused on prescription

**TABLE 1.** *Questions included in the WISDOM survey*

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Patients seen per month

- How many patients do you personally see and how many are women?
- What is the age distribution of your female patients?
- How many menopausal women are you personally involved in making treatment decisions?
- How many of the menopausal women that you manage or treat have vulvovaginal atrophy (VVA), including painful intercourse, vaginal dryness, vaginal itching and burning and/or bleeding with intercourse? Or vasomotor symptoms (VMS), including hot flashes and/or night sweats?

Treatments

- For your patients diagnosed with VVA, how do you treat them (no treatment, behavioral/lifestyle management only, over-the-counter products only, vaginal laser therapy only, prescription therapy with or without other therapies)?
- How many prescriptions for VVA do you write a month?
- What percent are for: Premarin vaginal cream, Estrace vaginal cream, Vagifem, Estring, Ospheana, compounded vaginal estrogen, DHEA, other?
- Rank the following reasons why you prescribe the VVA products: patient preference, patient out of pocket cost, effectiveness of product, ease of product use, physician preference, sample and sales support

Barriers to treatment

- Rank the following barriers to women treated for VVA: symptoms are not severe enough, fear of the risks associated with estrogen therapy, dissatisfaction with current therapies, out of pocket cost of treatment, other
- Rate the following reasons as to why women stop using their current VVA products: symptoms improved, symptoms don't improve with therapy or take too long to improve, messiness of the product, inconvenience of the product (need for an applicator, ring, other), cost, concern about long-term estrogen exposure

Attitudes toward treatments

- Rate your level of agreement for each of these statements concerning VVA treatment
- I believe my ability to treat VVA is limited by the choices currently available on the market
- VVA only requires treatment if the symptoms have a negative impact on the patient's quality of life
- VVA is best treated with OTC products rather than prescription products
- I prefer the use of localized estrogen therapies over other therapies
- I feel comfortable using localized estrogen therapy for menopausal women

How comfortable are you in using existing prescription therapy to treat VVA in women with

- No personal history or predisposition to breast cancer
- A predisposition to breast cancer (family history or *BRCA* mutations)
- A personal history of breast cancer

How important is it to be able to treat your patients that have VVA with the lowest effective dose?

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DHEA, dehydroepiandrosterone; OTC, over the counter; VMS, vasomotor symptoms; VVA, vulvovaginal atrophy.

therapies that have a primary indication for VVA treatment, such as local ET (creams, tablets, rings), dehydroepiandrosterone (DHEA), oral ospemifene; it does not include oral HT or ET. Panel members received \$23 in cash for completing the survey. Only completed surveys were included in the analysis. Responses were entered into an SPSS software package (SPSS, Inc, Chicago, IL) data file and summarized using crosstabs. Results were summarized, and responses between the two physician groups were compared and presented descriptively.

### Inclusion and exclusion criteria

The survey was conducted between August and September, 2016. Eligible survey participants included obstetricians and gynecologists (OB/GYNs), who saw at least 50 menopausal women per month, and primary care physicians (PCPs), who saw at least 25 menopausal women per month. PCPs were defined as physicians working in internal medicine, family practice, or general practice. Exclusion criteria were physicians who cited conflicts of interest, did not work in a US community-based practice, and managed or treated less than 15 patients with VVA per month.

## RESULTS

### Demographics

At least 2,424 physicians were invited to participate in the survey and 945 responded; 369 OB/GYNs and 275 PCPs completed the survey (27% completion rate). The majority of respondents were male (61% for OB/GYNs and 68% for PCPs), between 40 and 59 years of age (64%), and had been practicing for more than 15 years (66%; Table 2). On average, OB/GYNs and PCPs saw 111 and 99 menopausal women (mean age not known) per month, respectively; of these women, 61 (55%) and 44 (44%) were reported to have had VVA symptoms, and 64 (58%) and 51 (52%) were reported to have VMS symptoms, respectively.

### Attitudes toward VVA treatments

The most common VVA treatment recommended by physicians was prescription therapy (alone or in conjunction with other therapies), followed by OTC products alone, no treatment, behavioral/lifestyle management alone, and vaginal laser therapy alone (Fig. 1A). Overall, more OB/GYNs preferred to treat VVA with prescription therapy compared with PCPs (53% vs 43%) and wrote more prescriptions per month (44 vs 35 per month). Compared with PCPs, OB/GYNs prescribed more estradiol cream (Estrace vaginal cream; Allergan Pharmaceutical International Limited, Madison, NJ), 17 $\beta$ -estradiol vaginal tablets (Vagifem; Novo Nordisk Health Care AG, Plainsboro, NJ), oral ospemifene (Osphena, Duchesnay USA, Rosemont, PA), and estradiol ring (Estring, Pfizer, New York, NY), whereas PCPs prescribed more conjugated equine estrogen cream (Premarin vaginal cream, Pfizer, New York, NY) and compounded therapies (Fig. 1B).

Reasons why physicians prescribed VVA treatments (vaginal ET, DHEA, ospemifene; not OTC products) were similar

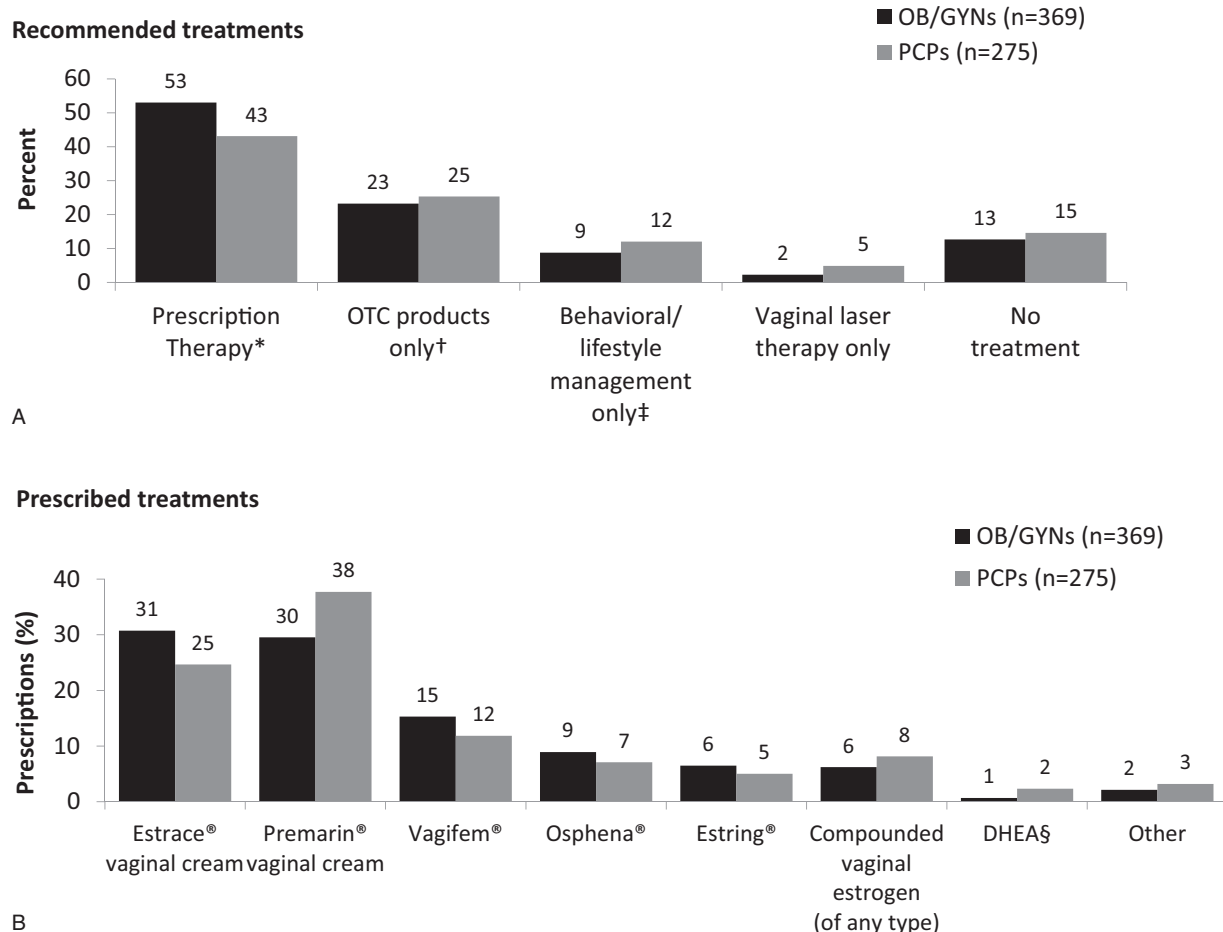
**TABLE 2.** Demographic characteristics of WISDOM survey respondents

Physician characteristic	OB/GYNs (n = 369)	PCPs (n = 275)
Sex		
Male	226 (61)	186 (68)
Female	143 (39)	89 (32)
Age, y		
<30	0	1 (0)
30-39	46 (12)	35 (13)
40-49	107 (29)	89 (32)
50-59	116 (31)	100 (36)
60-69	90 (24)	49 (18)
≥70	10 (3)	1 (0)
Years practicing postresidency		
0-5	22 (6)	15 (5)
6-10	39 (11)	37 (13)
11-15	59 (16)	49 (18)
16-20	71 (19)	50 (18)
>20	178 (48)	124 (45)
Primary practice setting		
Community office-based, solo private practice	50 (14)	40 (15)
Community office-based, group private practice	117 (32)	99 (36)
Community hospital-managed practice	23 (6)	18 (7)
Multi-specialty hospital system	0	0
Out-patient clinical associated with an academic/teaching hospital	0	0
Other	0	0

Data represented as n (%) unless otherwise indicated. OB/GYNs, obstetricians and gynecologists; PCPs, primary care physicians.

between OB/GYNs and PCPs, with the most common being effectiveness (77% and 76%, respectively), followed by patient out-of-pocket cost (33% and 34%), patient preference (28% and 30%), and ease of product use (29% and 28%). More OB/GYNs prescribed VVA treatments because of free sample availability for distribution and sales support from pharmaceutical companies than PCPs (18% vs 9%), whereas more PCPs prescribed them because of their personal preference (24% vs 15%). Out-of-pocket cost and fear of estrogen's risks were believed to be the main barriers for women choosing not to use prescription therapy, although these were followed closely by symptoms were not severe enough for treatment, and dissatisfaction with current therapies (Fig. 2A). OB/GYNs and PCPs also believed that the main reasons why women discontinue treatment were because of cost, symptom improvement, and concerns about long-term estrogen exposure (Fig. 2B).

Opinions of OB/GYNs and PCPs on statements about VVA treatments are in Table 3. Approximately 40% of OB/GYNs and PCPs agreed or strongly agreed with the statement that their ability to treat VVA was limited by the currently available choices and that VVA only required treatment if the symptoms negatively impacted a patient's quality of life. More OB/GYNs (72%) than PCPs (47%) disagreed or strongly disagreed that VVA was best treated with OTC products than prescription products; however, only 10% of OB/GYNs and 27% of PCPs agreed with the statement. Most



**FIG. 1.** (A) Treatment recommended by physicians to patients with VVA; (B) VVA treatments prescribed by physicians. \*With or without any other type of treatment; †vaginal lubricants and moisturizers; ‡increased sex, vaginal dilation, other; §intravaginal was not approved at the time of the survey. DHEA, dehydroepiandrosterone; OB/GYNs, obstetricians and gynecologists; OTC, over the counter; PCPs, primary care physicians; VVA, vulvovaginal atrophy.

OB/GYNs and PCPs agreed that they were comfortable prescribing local ET for menopausal women and that local ET were preferred over other types of therapies for VVA (Table 3). Overall, 84% of both OB/GYNs and PCPs queried considered it important to use the lowest effective dose of HT when treating women experiencing VVA symptoms; only 2% thought it was not important.

**Prescribing VVA therapies and breast cancer**

Almost all OB/GYNs (95%) and most PCPs (80%) agreed they felt comfortable prescribing existing VVA therapies (vaginal ET, DHEA, ospemifene) to women with no personal history or predisposition (family history or BRCA mutations); only 1% of OB/GYNs and 5% of PCPs were not comfortable or less comfortable doing so (Fig. 3A). In contrast, when asked about prescribing VVA therapies to women with a predisposition to breast cancer (family history, BRCA mutations, etc), 49% of OB/GYNs and 23% of PCPs felt comfortable doing so, whereas 23% of OB/GYNs and 44% of PCPs were not comfortable or less comfortable (Fig. 3B). Similarly, in women with a personal history of breast cancer, the

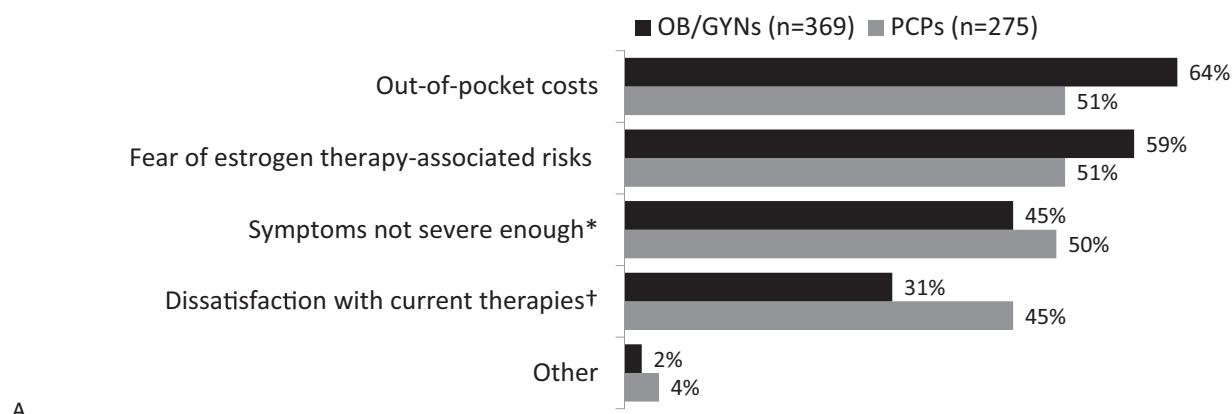
percentages dropped to 34% for OB/GYNs and 17% for PCPs; 39% of OB/GYNs and the majority of PCPs (61%) felt less comfortable or not comfortable doing so (Fig. 3C).

**DISCUSSION**

Overall, both OB/GYNs and PCPs had generally similar attitudes and behaviors regarding VVA treatment for menopausal women; but more OB/GYNs than PCPs prescribed VVA treatment, especially vaginal estrogens. Most physicians were comfortable prescribing vaginal ET for VVA and prefer it over other products. However, this comfort level lowered for prescribing VVA therapies for menopausal women with an elevated risk or personal history of breast cancer. As recommended by most medical societies, most physicians thought it was important to prescribe the lowest effective dose possible of US FDA-approved vaginal estrogens.

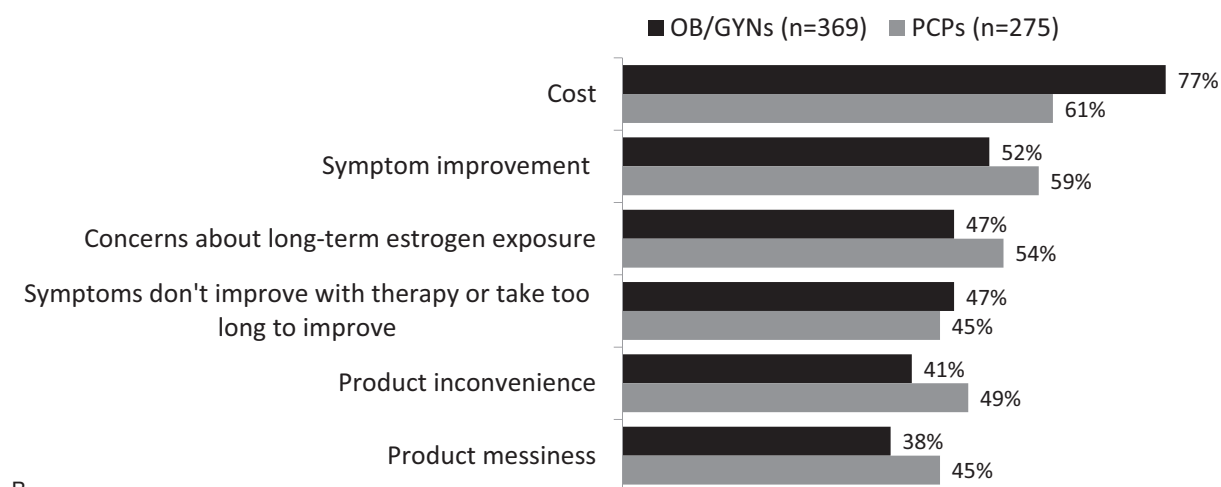
Physicians reported that patients had concerns over the safety of ET as a reason for not starting therapy, and also discontinuing treatment, which was consistent with other published studies. In the Women’s EMPOWER survey,

## Barriers to treatment



A

## Reasons for Discontinuation



B

**FIG. 2.** Physicians' perspectives on (A) barriers to prescription therapy; (B) reasons for discontinuing prescription therapy. Options were ranked 1 (primary reason) through 5 (least important reason). Options shown are those ranked 1 or 2 by each physician. \*Symptoms are not severe enough and patients prefer to deal with symptoms without prescription therapy; †applicators, discharge from products, dosing issues, and so on. OB/GYNs, obstetricians and gynecologists; PCPs, primary care physicians.

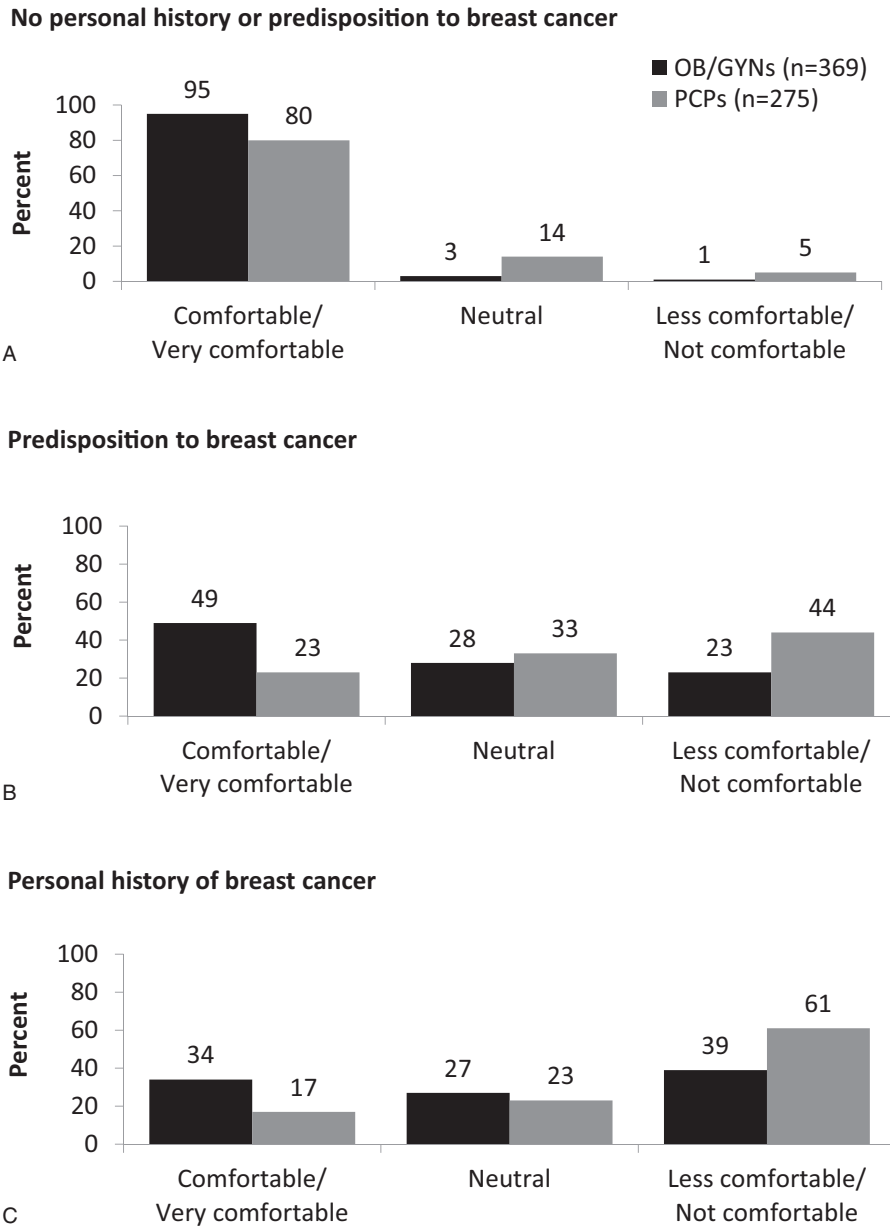
43% of women did not use hormonal products for VVA symptoms (such as vaginal ET) because of concern over risk of side effects, and 30% of women had concern over hormone safety in women with cancer or history of familial cancer.<sup>18</sup> In this same survey, women also stopped taking prescribed VVA products because they became concerned about the risks

(31%) and side effects (17%).<sup>18</sup> Other reasons for discontinuing prescribed VVA therapies cited by the Women's EMPOWER<sup>18</sup> and REal Women's Views of Treatment Options for Menopausal Vaginal ChangEs-Europe<sup>26</sup> surveys included symptoms stopped or were not bothersome enough to warrant an intervention, medication was not deemed to be

**TABLE 3.** Opinions of OB/GYNs and PCPs on statements about VVA treatments

Statements	OB/GYNs			PCPs		
	Agreed	Neutral	Disagreed	Agreed	Neutral	Disagreed
I believe my ability to treat VVA is limited by the choices currently available on the market	42	24	34	45	35	20
VVA only requires treatment if the symptoms have a negative impact on the patient's quality of life	39	26	35	40	31	29
VVA is best treated with OTC products rather than prescription products	10	18	72	27	26	47
I prefer the use of localized estrogen therapies over other therapies	75	15	10	68	16	16
I feel comfortable using localized estrogen therapy for menopausal women	87	4	9	65	16	19

Statements were rated on a scale of 1 through 5, with 1 corresponding to "strongly disagree" and 5 corresponding to "strongly agree". OB/GYNs, obstetricians and gynecologists; OTC, over the counter; PCPs, primary care physicians; VVA, vulvovaginal atrophy.



**FIG. 3.** How comfortable are OB/GYNs and PCPs prescribing VVA therapy to women with (A) no personal history or predisposition to breast cancer; (B) a predisposition to breast cancer, such as family history or a *BRCA* mutation; or (C) a personal history of breast cancer. VVA therapies included vaginal estrogen therapy, Osphe<sup>n</sup>a, Estring, DHEA, or other existing VVA products. DHEA, dehydroepiandrosterone; OB/GYNs, obstetricians and gynecologists; PCPs, primary care physicians; VVA, vulvovaginal atrophy.

efficacious, and the cost of the medication being too high. While the cost of treatment was cited in this survey as one of the most important barriers to treatment, in the Women’s EMPOWER survey, only 12% of women did not use prescribed VVA therapies because of high costs.<sup>18</sup> However, in REal Women’s VIEWS of Treatment Options for Menopausal Vaginal ChangEs-USA, 32% of women currently using vaginal ET had concerns about costs.<sup>16</sup>

While OB/GYNs and PCPs felt comfortable prescribing VVA therapies to women with no personal history of breast cancer, they felt less comfortable doing so in women with either an elevated risk or a personal history of breast cancer. These

results are similar to the ones obtained from Italian oncologists surveyed in 2015, which revealed that only 24% prescribed vaginal ET for patients with nonhormone-dependent breast cancer, and only 7.5% prescribed it to patients with hormone-dependent breast cancer.<sup>23</sup> Not surprisingly, a major concern of prescribing vaginal estrogens in breast cancer survivors is the potential risk of systemic exposure with potential for absorption and possible adverse breast effects.<sup>7,23</sup>

Multiple medical organizations have published clinical guidelines recommending that nonhormonal vaginal moisturizers and lubricants should be used as first-line treatment for breast cancer survivors.<sup>7,14,27</sup> While systemic HT and tibolone

are contraindicated in women with a history of breast cancer due to an increase in breast cancer recurrence,<sup>28-30</sup> medical societies, such as ACOG, NAMS, and IMS, support the short-term use of vaginal estrogens in women with a history of estrogen-dependent breast cancer who are unresponsive to nonhormonal therapies for the treatment of moderate-to-severe VVA.<sup>7,14,27</sup> In addition, such decisions should be made in consultation with their oncologist.<sup>7,14,27</sup> Although use of local or systemic menopausal ET for the treatment of VVA is currently contraindicated as per their prescribing information for women with known, suspected, or a history of breast cancer, these medical societies offer these recommendations because of the evidence suggesting the lack of or low systemic absorption of low-dose vaginal estrogens.<sup>31-38</sup> Furthermore, data do not show an increased risk of cancer recurrence in women with a history of breast cancer who use minimally absorbed local vaginal estrogen products for VVA symptoms.<sup>27,39,40</sup> A retrospective study of data from the US Cancer Surveillance System found that women with breast cancer had no increase in breast cancer recurrence with vaginal ET versus never use (relative risk 0.46, 95% confidence interval [CI] 0.21-1.01).<sup>39</sup> Similar results were observed in an analysis of the UK General Practice Research Database of women with breast cancer (n = 13,479), which found no increase in breast cancer recurrence with vaginal ET compared with non-users (relative risk 0.78, 95% CI 0.48-1.25).<sup>40</sup>

The use of low-dose vaginal ET for the treatment of moderate-to-severe VVA in women with a history of breast cancer may be considered based on several studies showing users with improved vaginal symptoms having very low to no systemic absorption of estradiol.<sup>41-46</sup> Systemic absorption can also be minimized with different estradiol formulations and if products are applied to the lower part of the vagina as compared with the upper part.<sup>43,47,48</sup>

Online surveys generally have several limitations, including self-reporting biases.<sup>49,50</sup> One limitation of this survey was that respondents were not randomly selected, but were chosen from a pool of physicians. While this pool was meant to be a nationally representative sample of physicians, physicians who like to complete market research surveys may be different from those who do not, and therefore results may not be applicable to the general physician population. The percentage of physicians who completed the survey could also be a limitation; while the number of completed surveys was not very high (27%), it was also not particularly low when compared with the completion rates other surveys (10%–41%) in the published medical literature.<sup>18,21,22,24</sup> In addition, the demographics of the respondents were fairly similar to the data of the 2016 Physician Specialty Data Report, which reported that males account for 46% of OB/GYNs and 62% of family medicine/general practice physicians in the United States, with the majority (56% and 58%, respectively) being under the age of 55.<sup>51</sup> Physicians who completed the survey also received an incentive, which could have affected how they answered the questions. Another limitation of this survey is that one of the questions inadvertently did not have

an answer that covered a popular option of prescription therapy use. Specifically, when surveying the physicians' attitudes regarding VVA treatments, "VVA is best treated with OTC products first, then prescription products," a recommended treatment option from medical societies, was not included as an answer. This survey had several strengths, including the fact that the GMI panel is compliant with research industry standards and uses various methods to remove any fraudulent survey answers. Overall, this survey provides a current perspective on physicians' behaviors and attitudes regarding VVA treatment in menopausal women.

## CONCLUSIONS

More OB/GYNs than PCPs prescribed VVA treatment, especially vaginal estrogens, for menopausal women, but overall, both types of physicians had generally similar attitudes and behaviors regarding VVA treatment. Most physicians preferred prescribing US FDA-approved vaginal ET at the lowest effective dose possible and were comfortable prescribing it. However, fewer were comfortable prescribing vaginal ET to women with an elevated risk or personal history of breast cancer, despite medical societies supporting its use in consultation with an oncologist when nonhormonal therapies fail to improve symptoms. Vaginal products that have negligible absorption of estradiol may be viable choices for these women, suggesting the need for more studies in this population.

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