

# The European Vulvovaginal Epidemiological Survey (EVES) in Italy. Impact of vulvovaginal atrophy on the quality of life and sexual function in breast cancer survivors

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The European Vulvovaginal Epidemiology Survey (EVES) sub-analysis assesses the impact of history of breast cancer (HBC) on vulvovaginal atrophy (VVA), sexual function and quality of life in a sample of postmenopausal women. Women aged 45-75 years with at least one symptom of VVA attending Italian menopause centers were included; subgroup data were described according to the absence (N = 967) or presence (N = 78) of HBC. VVA confirmed by gynecological examination and Vaginal Health Index < 15 was more prevalent in women with HBC (93.6% vs. 86.0% and 78.2% vs. 65.9%, respectively). Self-reported vaginal discharge, itching and urinary frequency were more prevalent in women without HBC compared to different HBC subgroups. Day-to-Day Impact of Vaginal Aging (DIVA) and sexual function scores were similar between women with or without HBC, but women who have completed breast cancer (BC) therapy showed lower sexual distress. Women with HBC had a higher vaginal prevalence and severity of signs of VVA, while self-reported VVA symptoms were generally less disruptive in women with HBC. These exploratory findings warrant confirmation in larger studies.

## Keywords

Breast cancer; Menopause; Gynecological examination; Quality of life; Sexual dysfunction; Vulvovaginal atrophy; Genitourinary syndrome of menopause

## 1. Introduction

Vulvovaginal atrophy (VVA) is a common condition in postmenopausal women and a key component of genitourinary syndrome of menopause (GSM), a collection of symptoms and signs associated with a decrease in estrogen and other sex steroids involving changes in the genitourinary area [1]. In approximately 50% of postmenopausal women, VVA leads to moderate or severe symptoms [2]. Vaginal dryness and dyspareunia associated with VVA are chronic and worsen progressively, contributing to sexual dysfunction, affecting quality of life (QoL) and intimate relationships. Despite this detrimental impact in terms of distress [3] and QoL [3, 4], postmenopausal women often consider these symptoms to be the normal outcome of ageing, discouraging them from consulting their health care provider and the symptoms are consequently underreported [5].

Women with a history of breast cancer (HBC), particularly if treated with aromatase inhibitors, have been shown to be more likely to have moderate or severe symptoms and signs of VVA than women without HBC [6]. Most adjuvant breast cancer (BC) therapies lower estrogen levels, which consequently induces VVA symptoms. Moreover, approximately 60% of premenopausal women become menopausal

during BC therapy, further exacerbating this problem. Postmenopausal BC survivors were more likely to report vaginal dryness (seven times) and pain during intercourse (five times) compared to premenopausal women [7].

The impact of VVA on the QoL of BC patients remains controversial [8–10]. BC survivors undergoing chemotherapy or entering menopause before the age of 50 have been reported to have poorer sexual functioning compared to those who were not receiving chemotherapy or were still menstruating, although this does not have any impact on their health-related QoL [11]. An Italian study showed that chemotherapy increased vaginal symptoms of dryness and dyspareunia and loss of libido more than tamoxifen, an effect which is particularly pronounced in women who were premenopausal at the time of diagnosis [12].

To our knowledge, there are no studies assessing the severity of VVA symptoms in women with HBC versus those without HBC. The European Vulvovaginal Epidemiology Survey (EVES) was the first attempting to address this question, because it combined questionnaires covering QoL and sex life, such as the 5-dimension EuroQoL (EQ-5D-3L), the Day-to-Day Impact of Vaginal Aging (DIVA) questionnaire, the Female Sexual Function Index (FSFI) or the Female Sexual Distress Scale-Revised (FSDS-R), with gynecological examinations and determinations of the Vaginal Health Index and the Vulva Health Index [13]. The evaluation of women attending gynecology clinics in Spain and Italy revealed that self-rated symptoms of VVA and its impact on QoL and sexual function were mostly comparable between women with or without HBC survivors, despite a higher prevalence of VVA and worse physical indicators in BC survivors. Our analysis is centered on women participating in the EVES from Italian centers, and aims to better understand the clinical and QoL context of BC survivors in this country in order to adapt their management to their real needs.

## 2. Patients and methods

### 2.1 Design and patients

The study population was part of a cross-sectional multinational survey of postmenopausal women aged 45 to 75 years who attended menopause or gynecology clinics [14]. A woman was defined as postmenopausal if it had been > 12 months since her last menstrual period. The current study was focused on postmenopausal women with and without HBC with at least one symptom of VVA. The study was conducted in 23 Italian centers in accordance with ICH Guidelines for Good Clinical Practice. This study was approved by the Independent Ethics Committees of the participating centers and consent to participate in this study was obtained by each participant before study inclusion.

### 2.2 Procedures

The study procedures have been described previously [13]. Briefly, women who were attending a menopause/gynecology center and had at least one symptom of VVA completed a four-part questionnaire. Information

about menopause status and the presence of VVA symptoms was collected. Women provided information about their lifestyle and VVA therapies, the severity of VVA symptoms and QoL (EQ-5D-3L, EQ visual analogue scale [VAS] [15] and DIVA [16]) and sexual functioning (FSFI [25] and FSDS-R [18]).

The health status was self-reported using EQ-5D-3L, with measures of mobility, self-care, activities of daily living, pain/discomfort and anxiety/depression, and a VAS (ranging from 0 to 100, 100 being the best imaginable health state).

Day-to-Day Impact of Vaginal Aging (DIVA) is a structured and self-administered questionnaire that evaluates the impact of vaginal symptoms such as vaginal dryness, soreness, irritation, and itching on the patient's day-to-day life. It scores four QoL dimensions related to vaginal symptoms (daily activities [5 questions], emotional well-being [4 questions], sexual functioning [9 questions] and self-concept and body image [5 questions]) by using a closed-answer Likert structure for each dimension (e.g. "What about your desire or interest in being in a sexual relationship?": "Not at all", "A little bit", "Moderately", "Quite a bit", "Extremely"). Total scores for each dimension of the scale are computed by calculating the average of scores for the corresponding individual items. The possible score range for all domain scales is 0 to 4, with higher scores denoting greater impact of vaginal symptoms [16].

The impact of VVA on sex life was evaluated by the self-reported FSFI and the FSDS-R questionnaires. The FSFI is a brief questionnaire measure which comprises 19 questions (with different answer choice scales) of sexual functioning in women over the past 4 weeks. It was developed for the specific purpose of assessing 6 domains of sexual functioning (evaluating desire [2 questions], arousal [4 questions], lubrication [4 questions], orgasm [3 questions], satisfaction [3 questions], and pain [3 questions] during sexual activity). Within each individual domain, a domain score of zero indicates that the subject reported having no sexual activity during the past month. The domain scores are obtained as the sum of points attributed to questions in that domain multiplied by the domain factor. The full-scale score ranges from 2 to 36. The FSDS-R is a 13-item questionnaire that assesses concerns and distress related to sexual activity during the previous 30 days. Women rated each item in terms of frequency from 0 (never) to 4 (always). Items were summed to create a total score ranging from 0 to 52, with higher scores indicating more sexually related distress [17, 18].

A gynecological examination was performed by the investigator to confirm VVA, and Vaginal Health Index [19] and Vulva Health Index [13] scores were calculated. The Vaginal Health Index Score is a tool that evaluates 5 parameters (vaginal elasticity, vaginal secretions, pH, epithelial mucous membrane, vaginal hydration), to obtain a final score that defines the degree of atrophy in the genitourinary tract by assigning a single score to each parameter. The total score ranges from 5 to 25, where scores < 15 indicate vaginal atrophy. The

**Table 1. Demographic characteristics (N = 1,045)-Subgroup analysis.**

	No HBC (N = 967)	HBC (N = 78)	Ongoing BC Tx (N = 39)	Compl. BC Tx (N = 39)	BC HT (N = 34)	BC ChT (N = 5)
Age (years), mean ± SD	59.0 ± 7.2	58.4 ± 7.4	55.5 ± 7.3	61.0 ± 6.3	55.8 ± 7.4	53.8 ± 7.4
Weight (kg), mean ± SD	65.7 ± 11.9	64.7 ± 10.6	64.1 ± 8.7	65.3 ± 12.3	64.5 ± 8.6	61.4 ± 9.5
Height (cm), mean ± SD	161.0 ± 6.2	161.9 ± 6.3	162.5 ± 5.8	161.1 ± 6.7	162.0 ± 5.9	165.8 ± 4.5
BMI (kg/m <sup>2</sup> ), mean ± SD	25.4 ± 4.6	24.7 ± 3.8	24.3 ± 3.2	25.0 ± 4.4	24.6 ± 3.2	22.2 ± 2.4
Time since menopause (years), mean ± SD	9.6 ± 7.3	10.0 ± 6.8	7.7 ± 6.7	12.3 ± 6.2	7.7 ± 6.3	7.4 ± 9.9

Abbreviations: BC, breast cancer; BMI, body mass index; ChT, chemotherapy; Comp., completed; HBC, history of breast cancer; HT, hormone therapy; SD, standard deviation; Tx, treatment.

Vulva Health Index evaluates the labia majora and minora, the urethra (caruncle, trauma and inflammation), the clitoris, the introitus, and elasticity, color, discomfort and pain during intercourse, as well as related aspects, such as excoriation/ulceration. The scale ranges from 0 to 3, where a score of 0 indicates a normal vulva, a score of 1 indicates mild vulva atrophy, a score of 2 indicates moderate vulva atrophy, and a score of 3 indicates severe vulva atrophy. The total score ranges from 0 to 24, and a total score over 8 or a score of 3 (severe) in at least one question indicates vulvar atrophy.

### 2.3 Statistical analysis

Participating women were divided into subgroups according to whether they had HBC or not. The women with HBC were further divided in subgroups according to whether they had an ongoing or completed BC therapy. Among those who completed BC therapy, subgroups were created according to the number of years since primary BC surgery ( $\leq 5$ , 6-10 and 11-20 years), while patients currently undergoing BC therapy were divided into subgroups depending on whether they were receiving hormonal therapy or chemotherapy.

For continuous variables, quantitative descriptive statistics were calculated, including the mean, range and standard deviation (SD). Categorical variables were summarized as counts and percentages.

## 3. Results

### 3.1 Demographic characteristics

From May 2015 to March 2016, a total of 2,403 postmenopausal women were enrolled in the EVES survey (1,177 in Spain and 1,226 in Italy). Of those enrolled in Italy with at least one symptom related to VVA and excluding 21 unknown women (N = 1,045), 78 (7.5%) had a medical HBC, half of them with an ongoing antineoplastic treatment (n = 39). Most of these women with ongoing BC treatment were receiving hormonal therapy (n = 34), while 5 were receiving chemotherapy (Fig. S1). Among women who had completed antineoplastic treatment (n = 39), the time since primary BC clinical treatment was most commonly between 6 and 10 years ago (n = 20), followed by between 11 and 20 years ago (n = 13), and  $\leq 5$  years (n = 6).

The baseline characteristics of different BC subgroups (ongoing BC therapy, completed BC therapy, completed BC

therapy with surgery  $\leq 5$ , 6-10 and 11-20 years ago) and women without HBC were described. As expected, women with ongoing BC therapy were younger ( $55.5 \pm 7.3$ ) (Table 1), while women with a BC surgery 11 to 20 years ago were older ( $65.4 \pm 4.0$ ) (Table S1) than women without HBC ( $59.0 \pm 7.2$ ). The mean ages in the other subgroups were similar (Table 1 and Table S1).

Time since menopause was similar in women with and without HBC, and ongoing BC (on hormonal or chemotherapy). The comparison by years since primary BC surgery showed a higher time since menopause in women who underwent breast surgery between 11 and 20 years ago than those who underwent surgery 6-10 years ago and  $\leq 5$  years ago (Table 1 and Table S1). Weight, height and BMI were also similar in all subgroups.

### 3.2 Main VVA symptoms

The frequency of self-reported VVA symptoms in each BC subgroup (ongoing or completed BC therapy, completed BC therapy with surgery  $\leq 5$ , 6-10 or 11-20 years ago) and women without HBC were described. The most common VVA symptoms in women with HBC (both ongoing or completed BC therapy) and without HBC (Table 2) were vaginal dryness and pain during intercourse, with comparable percentages ranging from 83.7 to 89.7% and from 53.8 to 62.2%, respectively. Other VVA symptoms revealed that women without HBC had a higher frequency of vaginal discharge compared to those with HBC (23.2% vs. 14.1%), and that they were more prone to have urinary frequency than those with ongoing BC therapy (35.4% vs. 15.4%) and had a higher itching frequency compared to those with completed BC therapy (38.1% vs. 20.5%) (Table 2). Comparable results were observed in the frequency of pain during exercise, bleeding during/after intercourse, burning or irritation, dysuria, recurring UTIs, postcoital cystitis, abdominal pain, urinary incontinence nor urgency (Table 2). However, when comparing subgroups according to years since breast surgery, the women who underwent surgery 11 to 20 years ago (N = 20) had a lower itching (15.0%) and urinary frequency (10.0%) compared to women without HBC (data not shown).

The severity of vulvovaginal discomfort symptoms, scored by the participants as absent, mild, moderate or severe, was also described (Table S2).

**Table 2. Self-reported VVA symptoms (N = 1,045)-Subgroup analysis.**

	No HBC (N = 967)	HBC (N = 78)	Ongoing BC Tx (N = 39)	Compl. BC Tx (N = 39)	BC HT (N = 34)	BC ChT (N = 5)
<b>VVA Symptoms, % (n)</b>						
Vaginal dryness	83.7 (809)	87.2 (68)	89.7 (35)	84.6 (33)	88.2 (30)	100 (5)
Pain intercourse/penetration	62.2 (601)	56.4 (44)	53.8 (21)	58.9 (23)	55.9 (19)	40 (2)
Pain during exercise	16.6 (161)	10.3 (8)	10.3 (4)	10.3 (4)	11.8 (4)	0 (0)
Bleeding during/after intercourse	15.9 (154)	14.1 (11)	10.3 (4)	17.9 (7)	11.8 (4)	0 (0)
Burning or irritation	56.2 (543)	53.8 (42)	53.8 (21)	53.8 (21)	50 (17)	80 (4)
Itching	38.1 (368)	25.6 (20)	30.8 (12)	20.5 (8)	32.4 (11)	20 (1)
Vaginal discharge	23.2 (224)	14.1 (11)	12.8 (5)	15.4 (6)	11.8 (4)	20 (1)
Urinary incontinence	34.2 (331)	26.9 (21)	23.1 (9)	30.8 (12)	20.6 (7)	40 (2)
Urinary urgency	34.1 (330)	25.6 (20)	23.1 (9)	28.2 (11)	23.5 (8)	20 (1)
Urinary frequency	35.4 (342)	19.2 (15)	15.4 (6)	23.1 (9)	17.6 (6)	0 (0)
Dysuria	11.3 (109)	5.1 (4)	2.6 (1)	7.7 (3)	2.9 (1)	0 (0)
Recurring UTIs	15.4 (149)	10.3 (8)	12.8 (5)	7.7 (3)	14.7 (5)	0 (0)
Postcoital cystitis	8.1 (78)	7.7 (6)	7.7 (3)	7.7 (3)	8.8 (3)	0 (0)
Abdominal pain	16.2 (157)	12.8 (10)	7.7 (3)	17.9 (7)	5.9 (2)	20 (1)

**Table 3. Severity of vaginal and vulvar atrophy and symptoms-Subgroup analysis.**

	No HBC (N = 967)	HBC (N = 78)	Ongoing BC Tx (N = 39)	Compl. BC Tx (N = 39)
Vaginal Health Index; mean $\pm$ SD	13.5 $\pm$ 3.5	12.3 $\pm$ 2.9	12.2 $\pm$ 2.8	12.3 $\pm$ 3.0
Vaginal atrophy (Vaginal Health Index < 15); % (n)	65.9 (626)	78.2 (61)	79.5 (31)	76.9 (30)
Vulva Health Index; mean $\pm$ SD	9.0 $\pm$ 4.6	9.6 $\pm$ 4.1	9.5 $\pm$ 3.7	9.7 $\pm$ 4.6
Severe vulvar atrophy <sup>B</sup> ; % (n)	54.7 (517)	56.4 (44)	56.4 (22)	56.4 (22)
Vaginal symptoms total score; mean $\pm$ SD	6.1 $\pm$ 4.6	6.3 $\pm$ 4.9	7.0 $\pm$ 5.1	5.5 $\pm$ 4.5
Vulvar symptoms total score; mean $\pm$ SD	2.9 $\pm$ 2.5	2.9 $\pm$ 2.8	3.3 $\pm$ 2.8	2.6 $\pm$ 2.8
Urinary symptoms total score; mean $\pm$ SD	2.8 $\pm$ 3.0	2.6 $\pm$ 2.7	2.6 $\pm$ 2.7	2.6 $\pm$ 2.8
All symptoms total score; mean $\pm$ SD	12.2 $\pm$ 8.5	12.1 $\pm$ 8.9	13.3 $\pm$ 9.2	11.0 $\pm$ 8.6

### 3.3 Vaginal and vulvar atrophy and sexual dysfunction

The study investigators confirmed the presence of VVA by physical examinations and evaluated the signs of VVA to calculate the Vaginal Health Index and Vulvar Health index. The prevalence of confirmed clinical evidence of VVA was higher in women with than in women without HBC (93.6% vs. 86.0%) (Table S3). The severity of VVA and associated symptoms were also described (Table 3). The mean Vaginal Health Index was higher and thus better in women without HBC (13.5  $\pm$  3.5) than in women with HBC (12.3  $\pm$  2.9), independently of whether they had an ongoing (12.2  $\pm$  2.8) or completed BC therapy (12.3  $\pm$  3.0). Moreover, the mean Vulva Health Index was lower (indicative of better vulvar health index) in women without HBC vs. those with HBC (with ongoing or completed BC therapy). The prevalence of vaginal atrophy, defined as a Vaginal Health Index < 15, was lower in women without HBC (65.9%) than in women with HBC, ongoing and complete BC therapy (78.2%, 79.5%, and 76.9%). Comparable results were observed in the mean score of vaginal, vulvar, urinary or overall symptoms.

### 3.4 Health status, quality of life and sexual dysfunction

Health status, QoL and sexual function were similar in women with or without HBC, while some differences were detected between women without HBC and those with com-

pleted BC therapy (Table 4). The mean self-reported health status on the EQ-VAS was 69.2 ( $\pm$  15.2) for women without HBC and 67.2 ( $\pm$  18.0) with HBC, 68.4 ( $\pm$  17.8) with ongoing and 66.1 ( $\pm$  18.3) with completed BC therapy. The mean EQ-5D-3L scores were also comparable across subgroups. The impact of vaginal symptoms on the patient's day-to-day life as measured by the DIVA instrument revealed a lower impact in women with completed BC therapy (0.683  $\pm$  0.585) than in women without HBC (0.950  $\pm$  0.660), while the impact in other subgroups was comparable. The mean sexual function score of these women, evaluated by the FSFI was comparable across all subgroups. However, sexual distress, defined as a FSFS-R score  $\geq$  11, was less prevalent in women with completed BC therapy (17.5%) than in women without HBC (36.2%), while being above 30% in the subgroup including all women with HBC (33.3%) or to those with an ongoing BC therapy (48.7%) (Table 4).

## 4. Discussion

Vulvovaginal atrophy has been described as a frequent and relevant problem for BC patients [20, 21]. The present study shows that women with HBC present a higher prevalence of VVA confirmed by clinical gynecological examination compared to women without HBC (93.6% and 86.0%, respectively). All women with ongoing chemotherapy or who



**Table 4. Health status and sexual function-Subgroup analysis.**

	No HBC (N = 967)	HBC (N = 78)	Ongoing BC Tx (N = 39)	Compl. BC Tx (N = 39)
Health Status EQ-VAS, mean ± SD	69.2 ± 15.2	67.2 ± 18.0	68.4 ± 17.8	66.1 ± 18.3
EQ-5D-3L overall score, mean ± SD	0.907 ± 0.102	0.922 ± 0.08	0.930 ± 0.067	0.913 ± 0.086
EQ-5D-3L overall score, mean ± SD	0.907 ± 0.102	0.922 ± 0.08	0.930 ± 0.067	0.913 ± 0.086
DIVA - total, mean ± SD	0.950 ± 0.660	0.854 ± 0.705	1.024 ± 0.778	0.683 ± 0.585
FSFI - total, mean ± SD	16.5 ± 9.9	15.4 ± 10.6	15.0 ± 9.9	15.7 ± 11.3
Female Sexual Dysfunction (FSDS-R score ≥ 11), % (n)	36.2 (350)	33.3 (26)	48.7 (19)	17.5 (7)
FSDS-R (total score), mean ± SD	9.7 ± 11.9	10.5 ± 14.0	14.4 ± 15.5	6.5 ± 11.2

*Abbreviations:* BC, breast cancer; NE, not evaluable (requirements for Chi-square test not given); Compl., completed; DIVA, Day-to-Day Impact of Vaginal Aging questionnaire; EQ-VAS, EuroQoL visual analogue scale, EQ-5D-3L, EuroQoL 5 dimension questionnaire 3rd version; FSFI, Female Sexual Function Index; FSDS-R, Female Sexual Distress Scale-Revised; HBC, history of breast cancer; SD, standard deviation; Tx, treatment.

underwent primary BC surgery ≤ 5 years ago had clinically confirmed VVA, but given the small number of women in these subgroups (N = 5 and 6, respectively), these data need to be interpreted with caution and no conclusion regarding differences could be drawn. The prevalence of VVA in our study was higher than reported elsewhere (~70% in BC survivors and 50% in women without HBC) [21], which could be due to the fact that we evaluated postmenopausal women actively seeking help for their symptoms at menopause and gynecology clinics [13]. This selection bias needs to be considered when interpreting the data, as extrapolation to the global population is difficult to control for such an underreported illness, due to the acceptance of VVA as a normal age-degeneration process and/or the shame involved for many women in discussing it with their health care providers [5].

Vaginal signs, such as the investigator-assessed Vaginal Health Index and vulvar signs determined by the Vulvar Health Index, were also more marked in women with HBC than in women without HBC, both for women with an ongoing or completed BC therapy. The prevalence of vaginal atrophy, defined as a Vaginal Health Index < 15, was higher in women with HBC, ongoing and complete BC therapy (78.2%, 79.5%, and 76.9%) than in women without HBC (65.9%).

Day-to-Day Impact of Vaginal Aging (DIVA) and sexual function scores were similar between women with or without HBC, but women who have completed breast cancer (BC) therapy showed lower sexual distress. Recently, minimal clinically important score differences measured using the DIVA instrument have been reported in a study in postmenopausal women treated with lose-dose vaginal estradiol, moisturizer or topical placebo [22]. In addition, in this study, no significant between-group differences were detected in the DIVA domain scores (mean differences, treatment vs placebo group from -0.0 to -0.3 point change) which are in line with the score differences between groups observed in our study.

Symptoms of VVA have been reported to be more prevalent and severe in women treated for BC than in the general postmenopausal population [20, 21]. This contrasts with

the current study, in which postmenopausal women with HBC and at least one VVA symptom reported a lower prevalence of most VVA symptoms, despite the clinical confirmed signs of vaginal atrophy being more prominent in this subgroup. Moreover, women with completed BC therapy were less prone to have some self-reported VVA symptoms such as itching, had a lower impact of VVA on their QoL (according to the DIVA questionnaire) and were less prone to experience sexual distress (defined as FSDS-R score ≥ 11), a criterion used to qualify sexual symptoms as sexual dysfunctions, when compared to women without HBC, despite their worse investigator-assessed Vaginal Health Index. Since self-reported symptoms, QoL and sexual functioning are subjective measures, the perception of women with HBC when comparing VVA with a life-threatening illness such as BC may partially explain these apparent contradictions. Indeed health-related QoL of cancer patients and the general population is difficult to compare, given the impact that living with cancer might have on life perception and changes in priorities [16]. As BC survivors adapt to their health situation, their responses in QoL questionnaires change, a phenomenon called response shift [23]. This shift might be due to either reconceptualization (the target construct was redefined), reprioritization (importance of the target's components has changed) or recalibration (internal standards have changed) [24]. Such a shift might certainly influence their responses in questionnaires which evaluate their perception of QoL and VVA symptoms when compared to women without HBC.

One limitation of the current study is the large imbalance in the number of participants with and without HBC, the first group being further divided (which further increases the imbalance) for subgroup analysis. This difference in the size of subgroups was anticipated, given the lower prevalence of women with compared to those without HBC. As mentioned earlier, the small sample sizes in some subgroups do not make it possible to draw conclusions regarding their comparability. However, the fact that the EVES combines gynecological examinations with self-reported questionnaires completed at

face-to-face visits makes it a powerful approach compared to other studies using only non-face-to-face surveys. These exploratory findings therefore warrant confirmation in larger studies.

## 5. Conclusions

The EVES compared VVA in postmenopausal women with and without HBC, by combined physical examinations and investigator-determined Vaginal and Vulvar Health Index with self-reported impact of VVA on QoL, health status and sexual function. These data are centered on women seen at Italian sites, and show a higher prevalence of VVA and worsened vaginal condition in postmenopausal women with HBC, while self-reported VVA symptoms were generally less disruptive for them. These apparently contradictory results suggest that women with HBC may have a less bothersome perception of VVA symptoms when set in a context of a life-threatening illness such as BC.

## Author contributions

REN designed the research study. REN, NB, EC, SL, MS and PV performed the research. All authors provided help and advice on the experiment. REN analyzed the data. All authors wrote the draft and supervised and revised for intellectual content. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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## Conflict of interest

Rossella E. Nappi has financial relationships (as a lecturer, member of advisory boards and/or consultant) with Astellas, Bayer-Schering Pharma, Endoceutics, Exceltis, Fidia, Gedeon-Richter, Merck Sharp & Dohme, Novo Nordisk, Palatin, Pfizer Inc., Shionogi Limited, and Theramex.

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Ettore Cicinelli declares no competing interests.

Tiziana Di Paolantonio is an employee of Shionogi Ltd.

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Paola Villa has financial relationships as lecturer and consultant with Alfasigma, PharmExtracta, and Shionogi.

## Supplementary material

Supplementary material associated with this article can be found, in the online version, at <https://ejgo.imrpress.com/EN/10.31083/j.ejgo.2021.01.2119>.

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