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## Impact of vulvovaginal atrophy of menopause: prevalence and symptoms in Italian women according to the EVES study

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### ABSTRACT

This cross-sectional study included postmenopausal women, aged 45–75 years, with the aim to assess the presence of vulvovaginal atrophy (VVA) confirmed by a clinical assessment in the Italian population attending menopausal/gynecological centers. Apart from baseline variables, women scored vaginal, vulvar and urinary VVA symptoms. Impact of VVA on sexual function and quality of life (QoL) was assessed thorough EuroQoL questionnaire (EQ5D3L), Day-to-Day Impact of Vaginal Aging (DIVA), Female Sexual Function Index (FSFI) and Female Sexual Distress Scale-revised (FSDS-R). A physical examination was carried out in accordance with routine gynecological practice. VVA was confirmed in 90% of the 1226 evaluable patients (aged  $59.0 \pm 7.3$  years). The prevalence of postmenopausal women with VVA confirmed by gynecological clinical assessment was 75.3%. The patients with VVA confirmed ( $n = 926$ ) had more severe symptoms ( $p < .0005$ ), lower QoL (EQ-visual analog scale,  $p = .008$  and DIVA,  $p < .0005$ ) and worsened sexual function (FSFI and FSDS-R,  $p < .0005$  for both) when compared with the patients having nonconfirmed VVA ( $n = 140$ ). VVA is highly prevalent among postmenopausal Italian women. The objective of VVA confirmation is associated with severe symptoms and impaired QoL and sexual function. A proactive approach of Italian clinicians to promote regular and early gynecological evaluation should be performed in order to delay the advancing of the disorder.

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### Introduction


Vulvovaginal atrophy (VVA) is a common chronic condition after menopause caused by a decrease in estrogen levels [1]. Estrogen levels play a significant role in maintaining thickness and urogenital territory moisture through the safeguarding of the mucopolysaccharide and mucosa collagen content [1]. This reduction in plasma levels led to changes in the lower genital and urinary tracts. In addition to the impact on sexuality, VVA has been shown to affect urinary function and it may interfere with daily living activities [2,3]. The associated group of VVA symptoms after postmenopausal estrogen deficiency is recently defined as Genitourinary Syndrome of Menopause [4] and includes dryness, irritation, soreness, and dyspareunia with urinary frequency, urgency and urge incontinence. Dyspareunia secondary to VVA is an important contributor to female sexual dysfunction. All these clinical symptoms are associated with major significant psychosocial distress [5] and reduced quality of life (QoL), with a considerable impact on women's daily living [5,6]. This is the reason why VVA is associated with comorbid cognitive-emotional factors, such as depression [7].

The global impact of VVA is low recognized by patients. In many cases menopausal women considered their vaginal symptoms as the normal consequence of age, as shown by a study on aging European population (55–65 years) [8]. The prevalence of menopausal women with symptoms of VVA has been reported to be about 50% [2,9] whereas the percentage of these patients with VVA confirmed by examination seems to oscillate between 67% and 98% [10]. In this sense, VVA clinical diagnosis is underreported, mostly related to the lack of understanding on how much VVA may impact the sexual health and the QoL of women and their partners. But attending that vaginal discomfort can become highly and clinically relevant, the disclosure of the VVA-related symptoms appears basic in order to improve management [2]. Similarly, when health care professionals (HCPs) are proactive and discussed VVA symptoms with women those are better treated and remained on treatment for more time [6].

Different treatments exist for VVA, depending on the postmenopausal symptoms, including local moisturizers, lubricants and estrogens, as well as systemic estrogen therapy. The Selective Oestrogen Receptor Modulator (SERM) ospemifene has appeared

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 Supplemental data for this article can be accessed [here](#).

in the last years for the treatment of moderate–severe symptomatic VVA in postmenopausal women who are not candidates for the treatment with local vaginal estrogens [11]. But despite these currently available therapeutic options, the burden of the VVA in menopausal women remains poorly controlled.

This *post hoc* analysis belongs to the European Vulvovaginal Epidemiology Survey (EVES) that assess the prevalence of postmenopausal women with VVA confirmed by gynecological clinical assessment among all postmenopausal women attending European menopause centers [12]. The main objective of the current study is to focus on the evaluation of the VVA presence in postmenopausal women confirmed even by a clinical assessment in the Italian population. The previous REVIVE experience in Europe (including Italy) evaluating attitudes and perceptions toward VVA used an online-based evaluation [13,14]. So, the current study including an individual survey together with a confirmatory gynecological examination provides a differential and innovative value for the characterization of this population of Italian postmenopausal women. Additionally, other aims included assessing the characterization of the VVA Italian population, and the overall impact of VVA on QoL and sexual functioning.

## Materials and methods

A cross-sectional study based on a survey addressed to postmenopausal women was performed in menopause centers or gynecological clinics in Italy and Spain. This *posthoc* analysis was focused on postmenopausal women (>12 months after the last menstrual period) aged 45 to 75 years old included only in Italian centers. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the participant centers. All patients provided written informed consent before study entry.

Women attending menopause or gynecological centers were asked to participate in the study, which comprised four different parts. First, investigators performed a menopause status assessment asking for symptoms related with VVA. No additional information was collected for women who did not complain of any VVA symptoms. Women with at least one VVA symptom were asked to complete following parts of the survey. Women were asked for demographic details, lifestyle, medical history and treatments. Also, they scored their symptoms of VVA, based on a list of 19 potentially VVA-related complaints, on a 4 score severity scale (absent, mild, moderate and severe). The VVA-related complaints were grouped in three main types of symptoms (vaginal, vulvar and urinary symptoms) and a score of severity was calculated for each group. They also completed a set of questionnaires for measuring impact of VVA on QoL and sexual function. The EuroQoL questionnaire (EQ5D3L) [15] measures mobility, self-care, daily-life activities, pain-discomfort and anxiety-depression and also includes a Visual Analogic Scale (VAS) for the today's health status. The Day-to-Day Impact of Vaginal Aging (DIVA) [3] questionnaire scores four QoL dimensions (daily activities, emotional well-being, sexual functioning and self-concept and body image). The patients also filled the Female Sexual Function Index (FSFI) [16] that measures sexual activity and the Female Sexual Distress Scale-revised 2005 (FSDS-R) that depicted sexual concerns and distress [17].

Finally, a gynecological clinical assessment on the presence of VVA was performed by the investigator consisting of a physical examination with additional tests carried out in accordance with routine gynecological clinical practice. The signs of VVA were

recorded in order to calculate the Vaginal Health Index [18] and the Vulva Health Index [19]. Vaginal Health Index scores overall elasticity, fluid secretion, aspect of epithelial mucosa and moisture all together between 5 and 25 with lower scores corresponding to more urogenital atrophy (<15 represents vaginal atrophy). Vulva Health Index scores the aspect of labia, urethra, clitoris, introitus as well as elasticity and pain during intercourse all together between 0 and 24 (higher scores corresponding with greater vulvar atrophy). If the Vulva Health Index is >8 or there is score of 3 (severe) in any category, vulvar atrophy is suggested.

In order to obtain a sufficiently representative sample size of the Italian postmenopausal women with VVA symptoms, we planned to recruit approximately 1000 patients in Italy for the completion of the survey. For continuous variables, descriptive statistics including mean, standard deviation (SD) and medians were used. Categorical variables were summarized as percentages. Relationship between confirmed or nonconfirmed diagnosis of VVA and demographic and clinical characteristics was performed with Chi-Square test. Quantitative variables were compared by Student-*T* tests.

## Results

From an initial sample of 2412 postmenopausal women enrolled in the EVES study, 1230 (51%) were recruited in Italian outpatient menopause or gynecological centers. Among them, 1226 women were included and evaluable for screening of symptoms (part A) whereas 1073 women complained of at least one symptom related to VVA. From them, 1066 filled in the questionnaires and had an objective gynecological exam (evaluable for parts B, C, D) (see [Supplementary Material 1](#)).

Mean age  $\pm$  SD of the included patients was  $59.0 \pm 7.3$  years and they had been in menopause for  $9.7 \pm 7.3$  years. Among them, 84.8% experienced a physiological menopause, 10.1% had a surgically induced menopause and 5.1% a menopause promoted by medication. 65.5% of patients were sexually active. The most frequent events in the gynecological history of the included population were abortion (30.0%), breast disease (20.0%) and hysterectomy (17.4%). In addition, chronic diseases were observed in 76.7% of the patients ([Table 1](#)). Demographic characteristics of the patients in subpopulations by confirmed or nonconfirmed VVA are listed in [Table 1](#), with statistically clear significant differences detected in age and time since menopause. Women whose VVA was confirmed by their physician ( $n = 926$ ) were on average 3 years older than those whose VVA was not confirmed ( $n = 140$ ) ( $p < .0005$ ). Similarly, they were under menopause for an average of two or more years ( $p = .002$ ). Patients with VVA confirmed also presented significantly higher rates of malignant breast disease (94 out of 926 [10.2%] vs 5 out of 140 [3.6%],  $p = .002$ ) and hysterectomy (18.3% vs 11.4%,  $p = .033$ ). In terms of menopausal treatments, patients with confirmed VVA reported less effectiveness of treatment to relief symptoms and lower levels of satisfaction compared to women with nonconfirmed VVA ( $p < .0005$ , in both the cases). In the group of women with VVA confirmed status, effectiveness of the treatment was reported as no relief, low or moderate by 61.7% of participants. Similarly, very low to moderate satisfaction with VVA treatment was acknowledged by 72.8% of participants with confirmed VVA. The main reason for not being satisfied enough with the treatment within the women with confirmed VVA was lack of efficacy (36.1%).

Table 1. Baseline characteristics of the patients<sup>a</sup>.

	With $\geq 1$ VVA symptom and VVA assessment (N = 1066)	With $\geq 1$ VVA symptom and VVA assessment (N = 1066)		<i>p</i> <sup>b</sup>
		Confirmed VVA (N = 926)	Nonconfirmed VVA (N = 140)	
Age (years), mean $\pm$ SD (median)	58.9 $\pm$ 7.2 (58)	59.3 $\pm$ 7.3 (58)	56.4 $\pm$ 6.2 (56)	<.0005
Age at last menstruation (years), mean $\pm$ SD (median)	49.3 $\pm$ 4.2 (50)	49.4 $\pm$ 3.9 (50)	48.5 $\pm$ 5.8 (50)	.078
Time since menopause (years), mean $\pm$ SD (median)	9.7 $\pm$ 7.3 (8)	9.9 $\pm$ 7.3 (8)	7.9 $\pm$ 7.0 (6)	.002
Type of menopause, %				
Natural	84.50%	84.00%	87.90%	.47
Induced by medications	5.30%	5.50%	3.50%	
Surgical	10.20%	10.50%	8.60%	
Body Mass Index, mean $\pm$ SD (median)	25.3 $\pm$ 4.5 (25)	25.3 $\pm$ 4.6 (25)	25.4 $\pm$ 5.0 (25)	.737
Relationship status, %				
Married	75.50%	76.20%	71.30%	.06
Single	7.60%	7.10%	10.60%	
Widowed	7.70%	8.20%	4.50%	
In a relationship	9.20%	8.50%	13.60%	
Education, %				
Elementary	22.20%	22.90%	18.00%	.355
High School	61.10%	60.90%	62.60%	
Graduate	16.70%	16.20%	19.40%	
Employment status (YES), %	51.60%	50.40%	59.40%	.048
Tobacco use (YES), %	15.10%	14.60%	18.10%	.287
Treatments, %				
None	66.20%	66.30%	65.70%	.231
At least one treatment used	35.60%	35.40%	36.40%	
N. of treatments used				
1	64.40%	29.20%	29.30%	
2	29.20%	5.70%	5.00%	
3	5.60%	0.50%	2.10%	
Nonhormonal therapy applied vaginally, %	27.10%	27.60%	23.60%	.747
Hormonal (estrogen-containing) vaginally, %	9.00%	9.40%	6.40%	.886
Hormonal (estrogen-containing) systemic, %	6.60%	5.20%	15.70%	.684
Effectiveness, %				
No relief	7.00%	7.10%	6.50%	<.0005
Low relief	22.70%	25.70%	6.50%	
Moderate relief	28.80%	28.90%	28.30%	
Good relief	32.80%	32.40%	34.80%	
High relief	8.70%	5.90%	23.90%	
Treatment period, %				
1 week or less	4.40%	4.80%	2.20%	.942
1–4 weeks	17.70%	17.70%	17.80%	
1–3 months	23.20%	23.40%	22.20%	
3–6 months	11.60%	11.30%	13.30%	
Over 6 months	43.00%	42.70%	44.40%	
Overall satisfaction with the treatment, %				
Very low satisfaction	5.30%	5.10%	6.30%	<.0005
Low satisfaction	21.30%	23.90%	6.30%	
Moderate satisfaction	41.60%	43.80%	29.20%	
High satisfaction	26.60%	23.20%	45.80%	
Very high satisfaction	5.30%	4.00%	12.50%	
Reason for not being satisfied, %				
Not effective enough	36.10%	35.80%	38.90%	.949
Worried about side effects	13.10%	12.70%	16.70%	
Too expensive	12.60%	12.70%	0.00%	
Difficult or unable to apply vaginally	3.70%	4.00%	11.10%	
Messiness of treatment	14.70%	14.50%	16.70%	
Other	19.90%	20.20%	16.70%	
Currently sexually active (YES), %	65.50%	64.70%	70.70%	.162
Intercourse (N/month), mean $\pm$ SD [Range]	3.2 $\pm$ 2.5 (2.0)	3.1 $\pm$ 2.5 (2.0)	3.4 $\pm$ 2.7 (2.0)	.553
Caucasian ethnic group, %	95.50%	95.20%	97.10%	.106
Childbirth (YES), %	82.50%	82.40%	82.90%	.768
Abortion/miscarriage, %	30.00%	30.20%	28.60%	.508
Chronic diseases (YES), % <sup>c</sup>	76.70%	76.60%	77.90%	.736
Hypertension	29.20%	25.00%	29.80%	
Hypercholesterolemia	19.20%	22.10%	18.80%	
Hypothyroidism	14.70%	13.60%	14.90%	
Osteoporosis	14.00%	14.30%	13.90%	
Anxiety	12.20%	17.10%	11.40%	
Arthrosis	10.60%	11.40%	10.50%	
Sleep disorders	10.50%	12.10%	10.30%	

(continued)

Table 1. Continued.

	With $\geq 1$ VVA symptom and VVA assessment (N = 1066)	With $\geq 1$ VVA symptom and VVA assessment (N = 1066)		<i>p</i> <sup>b</sup>
		Confirmed VVA (N = 926)	Nonconfirmed VVA (N = 140)	
Surgery for prolapse/urinary incontinence, %	4.10%	5.00%	4.00%	.62
Breast disease (YES), <i>n</i> %	213 (20.0%)	188 (20.3%)	25 (17.9%)	.449
If YES. Benign	99 (9.3%)	80 (8.6%)	19 (13.6%)	
If YES. Malignant	99 (9.3%)	94 (10.2%)	5 (3.6%)	.002
Hysterectomy, %	17.40%	18.30%	11.40%	.033

<sup>a</sup>Totals and percentages calculated among the total number of available responses for each variable.

<sup>b</sup>Nonconfirmed VVA vs confirmed VVA comparisons.

<sup>c</sup>Diseases with 10% or more are shown.

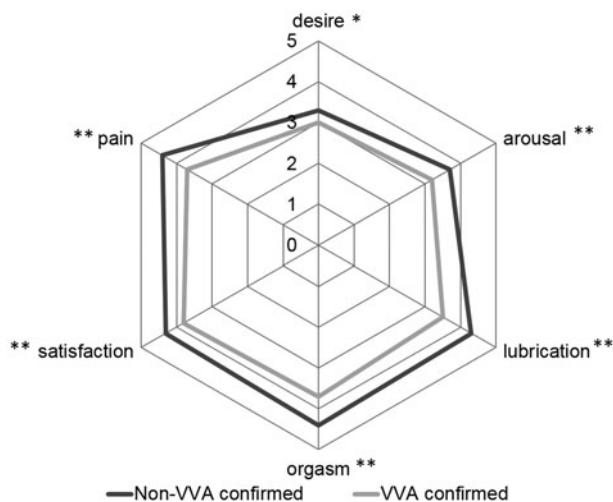


Figure 1. Domains of the FSFI score in the subpopulation of sexually active Italian women.

The prevalence of postmenopausal women with VVA confirmed by gynecological clinical assessment among all postmenopausal women attending menopause centers in Italy was 75.3% (926 out of 1230 enrolled women). The prevalence of women with at least one symptom related to VVA was 87.2% (1073 out of 1230). Among women with at least one symptom and having the assessments of VVA ( $n = 1066$ ), the mean number of symptoms was  $4.5 \pm 2.4$  (range: 1–14) and the most common symptom was vaginal dryness (84.1%) followed by pain during intercourse (61.5%; 69.6% among those women sexually active) and burning (56.1%) (Supplementary Material 2).

Table 2 shows main QoL, vulvovaginal discomfort and sexual function variables evaluated in the current sample. Score for severity was significantly higher in the VVA confirmed group as compared with the nonconfirmed VVA group for vaginal, vulvar, urinary symptoms as well as for the total symptom score. Mean Vaginal Health Index was significantly lower in women whose VVA was confirmed (12.8 vs 17.7,  $p < .0005$ ) and overall, vaginal atrophy as defined by a Vaginal Health Index  $< 15$  was wide more prevalent in VVA-confirmed women (74.9% vs 15.1%,  $p < .0005$ ). Mean Vulva Health Index was higher in women whose VVA was confirmed (9.8 vs 4.2,  $p < .0005$ ) as well as severe vulvar atrophy (62.3% vs 5.0%,  $p < .0005$ ). Confirmation of VVA by the physician following vaginal examination was associated with a significant lower current health state as shown by the EQ-VAS scores. In case of the DIVA, women whose VVA was confirmed had greater impact of vaginal symptoms. This trend was maintained evaluating the difference within the sexually active patients ( $n = 698$ ) (DIVA total: 1.0 vs 0.8,  $p < .0005$ ).

The impact on the sexual function was significantly higher in sexually active patients with VVA confirmed vs nonconfirmed VVA for the overall FSFI score (higher FSFI scores indicate better sexual function) (20.4 vs 24.2;  $p < .0005$ ) and for the six FSFI particular components (Figure 1). Also, significant differences between Italian sexually active women with confirmed and nonconfirmed VVA were detected for the overall FSDS-R (10.7 vs 6.6,  $p < .0005$ ) and also for the percentage of patients with severe FSDS-R score ( $\geq 11$ ) (40.1% vs 25.3%,  $p = .005$ ). The same trend were observed for these questionnaires comparing both VVA subpopulations within the global population (not only in the sexually active women; Table 2).

## Discussion

The current cohort analysis shows that the overall prevalence of VVA, confirmed by gynecologic assessment in postmenopausal women from Italy, reaches 75%. This result goes in agreement with the previous Italian AGATA study by which the prevalence of VVA under objective clinical exam in Italian postmenopausal women was 79%, ranging from 65% at one year after menopause to 84% six years later [20]. Equal than the AGATA study, at the time of the current evaluation, our sample was under menopause a mean of 10 years. The type of menopause of both studies was also similar (mostly physiological menopause, 83–85% in both the cases).

The prevalence distribution of the subjective symptoms of VVA seems to be slightly dependent on the evaluated sample, but maintaining the same trend. Within the studies evaluating Italian samples, the most reported VVA subjective symptom was vaginal dryness (84% in our sample, 77% in the AGATA study [20] and 78% in the REVIVE study [13]), followed by dyspareunia (62% in ours [70% in sexually active women] and AGATA study [20] and 76% in the REVIVE study [13]). Burning was reported in the 56% of our sample, while the AGATA prevalence of burning was 42% [20].

The previous VIVA online survey [8] based on population living in Great Britain, the United States, Canada, Sweden, Denmark, Finland or Norway reported global prevalences of vaginal dryness around 83% among women with vaginal discomfort, dyspareunia around 42% and burning around 14%. Also, they found that women's views and perceptions of vaginal atrophy and its symptoms varied geographically. Different ideas arise from here. First, the objective–subjective symptom differences scenario remarks the need of adequately assess the specific impact of this condition in postmenopausal women, through the use of well-established clinical tools, preferably by an objective clinical evaluation to confirm diagnosis and symptoms. Second, and in line with the overall EVES study [12], our data in Italy show that the presence of VVA symptoms in postmenopausal

**Table 2.** Comparison of questionnaires between VVA confirmed and VVA not confirmed.

	With $\geq 1$ VVA symptom and VVA assessment (N = 1066)	Confirmed VVA (N = 926)	Nonconfirmed VVA (N = 140)	<i>p</i> <sup>a</sup>
EuroQol-EQ5D3L, mean $\pm$ SD (median)	0.909 $\pm$ 0.101 (0.945)	0.907 $\pm$ 0.103 (0.945)	0.923 $\pm$ 0.087 (0.945)	.074
Health status (EQ VAS), mean $\pm$ SD (median)	69.1 $\pm$ 15.4 (70)	68.6 $\pm$ 15.0 (70)	72.4 $\pm$ 17.3 (75)	.008
DIVA total, mean $\pm$ SD (median)	0.943 $\pm$ 0.667 (0.847)	0.975 $\pm$ 0.670 (0.889)	0.734 $\pm$ 0.607 (0.559)	<.0005
FSFI total, mean $\pm$ SD (median)	16.4 $\pm$ 9.9 (18.4)	15.9 $\pm$ 9.7 (17.8)	19.9 $\pm$ 10.7 (23.9)	<.0005
FSDS-R total, mean $\pm$ SD (median)	9.8 $\pm$ 12.1 (4.0)	10.3 $\pm$ 12.3 (5.0)	6.6 $\pm$ 9.9 (2.0)	<.0005
Female sexual dysfunction (FSDS-R $\geq 11$ )	35.8%	37.7%	23.6%	.001
Severity of symptoms <sup>b</sup>				
Vaginal symptoms total score, mean $\pm$ SD (median)	6.1 $\pm$ 4.6 (5)	6.4 $\pm$ 4.7 (6)	4.0 $\pm$ 3.4 (3)	<.0005
Vulvar symptoms total score, mean $\pm$ SD (median)	3.0 $\pm$ 2.5 (2)	3.1 $\pm$ 2.6 (3)	2.0 $\pm$ 2.2 (1)	<.0005
Urinary symptoms total score, mean $\pm$ SD (median)	2.8 $\pm$ 3.0 (2)	2.8 $\pm$ 3.0 (2)	2.4 $\pm$ 2.4 (2)	.044
All symptoms total score, mean $\pm$ SD (median)	12.2 $\pm$ 8.5 (10)	12.7 $\pm$ 8.6 (11)	8.6 $\pm$ 6.2 (7)	<.0005

<sup>a</sup>Nonconfirmed VVA vs confirmed VVA comparisons.

<sup>b</sup>The VVA-related complaints were grouped in three main types of symptoms as follows: Vaginal symptoms included vaginal dryness (inside), pain during intercourse (inside), pain during intercourse at penetration, bleeding during intercourse, bleeding during sexual contact, burning or irritation (inside), itching (inside) and vaginal discharge. Vulvar symptoms included vaginal dryness (outside), burning or irritation (outside), itching (outside) and pain during exercise. Urinary symptoms included urinary incontinence, urinary urgency, urinary frequency, urinary difficulties, recurrent urinary tract infections and postcoital cystitis. In addition abdominal pain was recorded as an independent symptom.

women visiting a gynecology/menopause clinic is clearly higher than other studied populations cohorts; however, vaginal dryness, pain during intercourse and burning are the most subjective reported VVA symptoms across studies. In this sense, the REVIVE survey experience evaluating regional differences in Italy in terms of VVA symptoms [14] found no regional variances in most of them. Thus, country-specific approaches may be required to better distinguish patterns rather than regional population differences within a country. Third, the prevalence of VVA symptoms in some subgroups of women can be much higher. That is, in the case of survivors of breast cancer there is a clear relationship between this condition and the VVA symptoms presence [21]. In our Italian cohort, malignant breast disease was significantly higher in women with confirmed VVA than in nonconfirmed VVA (10.2% vs 3.6%). So, a personalized approach should be performed in specific subpopulations. The current Italian sample experienced a mean of 5 VVA symptoms, similar to other European samples.

The current data in Italian postmenopausal women support the already mentioned idea that VVA symptoms are strongly associated with sexual function and QoL impairments [2,9,22–24]. In the present cohort, sexually active women with VVA confirmed presented a worse sexual function (both by the global FSFI score and its components and the FSDS-R score). The previous REVIVE survey already postulated VVA symptoms that clearly interfered sexual activities (i.e. spontaneity, intimacy, sexual satisfaction) [5] in United States population; the 59% of women reported a high impact of VVA symptoms on sex enjoyment that become worse as the years under menopause increased [5]. The European REVIVE survey reported that although 75% of participants were still sexually active, this activity had been reduced by one-third because of VVA [13]. For the Italian population specifically, VVA symptoms had a significant impact on these participants' ability to achieve pleasurable relations (74%) and spontaneity (70%). Similar trends were confirmed for the Spanish population of the REVIVE study [19]. This goes in agreement with the idea that vaginal dryness is related to pain during intercourse and sexual functioning impaired [25].

Vaginal discomfort has been related to self-esteem and emotional well-being impairment among postmenopausal women [26]. Regarding the VVA impact on QoL in Italian postmenopausal women, we found that confirmed VVA was associated to a lower general health state (EQ-VAS). Data for the EuroQol-EQ5D3L provided no significant results. The DIVA results evaluating specific vaginal symptoms went in the same way; those women with confirmed VVA had greater impact on vaginal symptoms. The impact on the sexual function was significantly higher in sexually active patients with VVA confirmed vs nonconfirmed VVA both for the FSFI and FSDS-R scores. Our postmenopausal women with confirmed VVA reported problems in all the FSFI domains (desire, pain, satisfaction, orgasm, lubrication and arousal) showing a global impact on sexual function. The distress represented in the FSDS-R results coincides with previous results of the REVIVE survey, which showed that some postmenopausal Italian women reported anxiety (11%), worries (11%), frustration (15%) and depression (10%) in front of VVA symptomatology [13]. Score for severity was significantly higher in the VVA confirmed group as compared with the nonconfirmed VVA group for vaginal, vulvar, urinary symptoms as well as for the total symptom score. This also corresponded to the presence of vaginal and vulvar atrophy in the VVA confirmed group.

In total, our data suggest that an objective physical exam for VVA confirmation in early stages is key to prevent a future impact in QoL and sexual function domains in postmenopausal women, as a non-negligible 13% of our Italian sample showed a nonconfirmed VVA. However, they reported most of the subjective VVA symptoms with the same percentage than the confirmed VVA group. Despite the VVA significant impact on QoL, the condition remains underdiagnosed and undertreated in Italy. In the AGATA study the prevalence of women under therapies for VVA was low (28%) [27], compared with 58% reported in the REVIVE survey [13]. Our data show that the 66% of women with at least one symptom of VVA receive no treatment. Also, the effectiveness and overall satisfaction of the treatment were significantly higher in the case of the nonconfirmed VVA group

vs the confirmed one. This highlights the idea that an early treatment approach may prevent worsening of symptomatology joining a gynecological objective examination to confirm diagnosis and to discard alternative reasons for symptoms. The AGATA study considered that satisfaction with current treatments needs to be improved. It has been reported that local estrogen treatment improved relationships, particularly in Southern Europe [26]. While a 17% of the global population in the AGATA study used vaginal therapies [27] in 2016, in our current study this percent doubled (36%). In global terms, only 27% of the VVA confirmed group show high or very high satisfaction with therapy, while in the nonconfirmed VVA this percentage was of 58%. This reinforces the idea of a proactive early treatment in early phases of the disease. In the REVIVE study in patients who completed their local estrogen prescription or were currently taking it, 51% showed global satisfaction [13].

Finally, despite this is a face-to-face evaluation of VVA in postmenopausal women in Italy including an objective gynecological evaluation, compared with the previous online surveys, there is an inherent bias in the current sample associated with the exclusive evaluation of women asking for medical care.

In conclusion, the current Italian sample not only presents a high prevalence of confirmed VVA by an objective evaluation, but also high prevalences of the most common subjective symptoms that are reported in postmenopausal samples. Although many Italian women showed at least one symptom, VVA was not objectively confirmed on 13%. Attending the clear impact of VVA on QoL and sexual function and the beneficial effects of an early treatment, we advocate for a proactive approach of Italian clinicians to promote regular gynecological evaluations in perimenopause women without any evident signs in order to slow down the advancing of the condition.

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