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To cite this article: Rossella E. Nappi, Martire Particco, Nicoletta Biglia, Angelo Cagnacci, Costantino Di Carlo, Stefano Luisi & Anna Maria Paoletti (2017): Macro-regional variation in attitudes toward and experiences of vulvar and vaginal atrophy among Italian post-menopausal women: a post hoc analysis of REVIVE survey data, *Gynecological Endocrinology*, DOI: [10.1080/09513590.2017.1284783](https://doi.org/10.1080/09513590.2017.1284783)

To link to this article: <http://dx.doi.org/10.1080/09513590.2017.1284783>



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Published online: 21 Feb 2017.



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## ORIGINAL ARTICLE

# Macro-regional variation in attitudes toward and experiences of vulvar and vaginal atrophy among Italian post-menopausal women: a *post hoc* analysis of REVIVE survey data

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## Abstract

Italian participants in the European REVIVE survey reported that vaginal and vulvar atrophy (VVA) impaired various aspects of their lives, notably the ability to enjoy sex. The aim of the present study was to explore regional differences in knowledge, experiences, and treatment of VVA in the Italian REVIVE sample ( $n=1000$ ), which was analyzed according to region of residence. While many respondents were unfamiliar with the VVA condition, most could relate their VVA symptoms to the menopause. The rate of diagnosis of VVA was twice as high in Central Italy as in the North-East. For individual VVA symptoms, 25.4–41.6% of respondents judged that the symptom had worsened over time. There were no significant regional differences for symptoms in terms of reported rate, change in severity, impact on sexual activity, or health-care visits. Testosterone cream and OTC medication based on hyaluronic acid showed significant regional differences in lifetime rates of use. In Italy, there are modest regional differences in knowledge, diagnosis, and treatment of VVA, some of which may be explained by inter-regional differences in health care. Further efforts are needed to ensure that Italian women are properly informed about VVA and have access to appropriate health care and treatments.

## Introduction

Vulvar and vaginal atrophy (VVA) is a chronic condition associated with the dramatic reduction in estrogen levels at the menopause, which is now part of the genitourinary syndrome of menopause [1]. It is characterized by vaginal dryness and itching, pain during sexual intercourse, urinary urgency and urge incontinence, symptoms which can worsen over time [2,3]. While it is hard to accurately estimate the prevalence of VVA, US and European survey data from the last 10 years gave figures ranging from 38 to 54% [4–6]. These and other data confirm that VVA remains a major public health problem.

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## Keywords

Dyspareunia, Italian post-menopausal women, REVIVE survey, sexual relationships, vaginal dryness, vulvar and vaginal atrophy

## History

Received 21 December 2016

Accepted 17 January 2017

Published online 14 February 2017

VVA has a considerable negative impact on quality of life (QoL) [6,7]. In Women's Voices in the Menopause, an international survey of women aged 55–65, 40% of respondents reported that vaginal discomfort had worsened their sex life [8]. It had also negatively affected their self-esteem (17%), marriage/relationship (13%), and social life (7%). In a second international survey of postmenopausal women – Vaginal Health: Insights, Views & Attitudes (VIVA) – three-quarters of respondents expressed a negative effect of VVA on QoL [9]. Impairment of sleep or of general enjoyment of life was reported by just under a quarter of respondents in REal women's Views of treatment options for menopausal Vaginal changeEs (REVIVE), a large US survey [5].

When the US REVIVE survey was replicated in Europe (Italy, Germany, Spain, and the UK), over two-thirds of the women who had ever had VVA reported a negative effect on their sex life [2]. In spite of this, only 45% of respondents were receiving treatment at the time of the survey, and many expressed dissatisfaction with VVA treatments. Indeed, VVA is under-treated for a number of reasons, including embarrassment at seeking professional medical help and safety concerns over the long-term use of estrogen [8,10,11], which is effective at relieving VVA symptoms [12].

The European REVIVE study [2] and other international studies [8,9,13,14] reveal cultural differences in the impact of VVA on female sexuality and relationships. A recent European interview- and survey-based study further identified personality traits as an important factor influencing women's attitudes and behavior regarding VVA [15]. Nonetheless, the global picture is one of widespread discomfort and unrelieved suffering.

A recent analysis of the REVIVE data from Italy found that VVA reduced enjoyment of sex in 75% of respondents [3]. A majority of the respondents had expected their physician to initiate a discussion about sexual health after the menopause, but this rarely happened. For this reason, perhaps, less than 10% of the women currently receiving treatment were using a prescription medication; the vast majority were using over-the-counter (OTC) medications [3]. The AGATA Study also refers to Italian postmenopausal women, finding that almost 30% had had a previous diagnosis of VVA and were treated either with no therapy (10%), systemic hormone (9%), local hormone (45%), or local non-hormonal (37%) therapy [16].

The objective of the present analysis was to explore regional differences in experiences of VVA among Italian women included in the European REVIVE survey.

## Methods

Conducted in 2014, the European REVIVE survey [2] used the same methodology as the original US REVIVE survey [5]. Briefly, women aged 45–75 years and living in Italy, Germany, Spain, or the UK were screened for eligibility based on cessation of menstruation, menopause, and lifetime history of VVA symptoms. An invitation to participate has been sent to postmenopausal women with current or previous VVA. Participants completed an online questionnaire that lasted approximately 35 min. The questionnaire, which had been translated from the US REVIVE questionnaire and adapted culturally, was accessed via a secure online portal. To ensure that the questions could be fully understood, it was initially tested in a subsample of 50 participants.

The survey was approved by the relevant independent Ethics Committees, and all participants provided informed consent. As remuneration for their participation, participants received points that could be exchanged for vouchers or gadgets, but not money.

Participants provided information on the following: knowledge about VVA and menopausal symptoms, interactions with health-care providers (HCPs) regarding VVA symptoms, impact of VVA symptoms on sex life and activities of daily living, lifetime and current use of different treatments for VVA, and attitudes toward VVA treatments. Those who fulfilled all the screening criteria and who had valid data for the analyzed variables were considered eligible.

European REVIVE data for Italy alone were used in the present study. In total, 7284 of the 32 384 women who were screened and 1000 of the 3768 eligible participants were from Italy [3]. The Italian sample covers all regions of Italy in a demographically balanced manner: North-East (19.0% of the sample), North-West (33.8%), Central (20.9%), South (18.0%), and Islands (8.3%). The REVIVE study variables were analyzed according to geographical region.

Descriptive statistics were calculated without imputation of missing values. Relative frequency distributions are presented for categorical variables. Pearson's chi-squared tests with a 0.05 significance level were performed to detect differences by region in the frequencies of the survey responses.

## Results

### Demographics

Baseline demographics of the 1000 European REVIVE participants from Italy are presented elsewhere [3]. Briefly, nearly two-thirds of the participants were aged 51–60 years; none of them had menstruated in the previous 12 months. Most participants (79%) had received previous treatment for VVA, and 58% were receiving treatment at the time of the survey. Notably, there were regional differences in age distributions ( $p=0.029$ , Pearson's chi-squared test), with higher proportions of participants aged 71+ years in North-East (4.7%) and South Italy (3.3%) compared to other regions (0.5–1.2%) (Table 1). Marital status, occupational status, education, number of children, and having children living at home also showed significant regional differences ( $p<0.05$ ).

### Awareness of VVA and its causes

Overall, 415 of the 1000 participants reported being not at all familiar with VVA as a condition, with the proportion ranging from 40.0% in the South to 42.6% in Central Italy; 5.4% of participants reported being extremely familiar with VVA (range 3.3% [Central] to 7.2% [Islands]). In spite of this regional variation, Pearson's chi-squared test results indicated no significant differences ( $p=0.254$ ). Over half of the participants specifically mentioned the menopause when asked what they believed to be the cause of their VVA symptoms.

### VVA symptoms

The commonest VVA symptom experienced by the Italian REVIVE participants was vaginal/vulvar dryness, with an overall rate of 77.7% (range 69.9% [Islands] to 81.8% [Central]) (Figure 1A). In fact, vaginal/vulvar dryness was the most frequently reported menopausal symptom, ahead of hot flushes (75.1%), night sweats (61.4%), and weight gain (60.0%). However, there were no significant regional differences in vaginal/vulvar dryness rate ( $p=0.108$ , Pearson's chi-squared test). Pain during intercourse (30.5%) and vaginal/vulvar irritation (29.5%) were also frequently reported, although rates of these VVA symptoms did not differ significantly between different geographical regions ( $p=0.251$  for pain during intercourse and  $p=0.240$  for vaginal/vulvar irritation). Vaginal/vulvar pain/soreness was reported less frequently (8.2%) and showed no significant regional variation ( $p=0.499$ ).

Generally, participants found their VVA symptoms very bothersome. The following proportions of participants reported their symptoms as "extremely bothersome": vaginal/vulvar dryness, 33.5%; pain during intercourse, 59.0%; vaginal/vulvar irritation, 45.1%; and vaginal/vulvar pain/soreness, 42.7%. While the proportion of sufferers describing their vaginal/vulvar pain/soreness as extremely bothersome varied between 35.7% (North-East and South) and 60.0% (Islands), there were no significant regional differences in how bothersome the participants found any of their VVA symptoms ( $p>0.05$ ).

Interestingly, reported rates of VVA diagnosis showed significant regional variation ( $p=0.003$ ), ranging from 13.7% in the North-East to 29.7% in Central Italy (Figure 1B).

Participants were asked about the severity of their VVA symptoms at the time of the survey compared to when the symptoms first arose. Of the 777 participants who reported vaginal/vulvar dryness, 211 (27.2%) felt that it had worsened. There were no regional differences ( $p=0.757$ ). Pain during intercourse had worsened in 127/305 participants (41.6%), vaginal/vulvar irritation in 75/295 participants (25.4%) and vaginal/vulvar pain/soreness in 29/82 participants (35.4%). There were no significant geographical differences ( $p>0.05$ ).

Table 1. Baseline demographic data for the Italian REVIVE participants.

	North-West	North-East	Central	South	Islands	All regions	Pearson
<i>Age (years), n (%)</i>							$p = 0.029^*$
45–50	30 (8.9)	24 (12.6)	20 (9.6)	15 (8.3)	10 (12.0)	99 (9.9)	
51–55	113 (33.4)	59 (31.1)	59 (28.2)	67 (37.2)	27 (32.5)	325 (32.5)	
56–60	99 (29.3)	47 (24.7)	85 (40.7)	53 (29.4)	25 (30.1)	309 (30.9)	
61–65	76 (22.5)	36 (18.9)	32 (15.3)	28 (15.6)	14 (16.9)	186 (18.6)	
66–70	16 (4.7)	15 (7.9)	12 (5.7)	11 (6.1)	6 (7.2)	60 (6.0)	
71–75	4 (1.2)	9 (4.7)	1 (0.5)	6 (3.3)	1 (1.2)	21 (2.1)	
<i>Marital status, n (%)</i>							$p = 0.038^*$
Married	213 (63.0)	125 (65.8)	137 (65.6)	132 (73.3)	66 (79.5)	673 (67.3)	
Cohabiting	30 (8.9)	17 (8.9)	10 (4.8)	12 (6.7)	2 (2.4)	71 (7.1)	
Separated	12 (3.6)	10 (5.3)	8 (3.8)	7 (3.9)	3 (3.6)	40 (4.0)	
Divorced	32 (9.5)	13 (6.8)	26 (12.4)	8 (4.4)	6 (7.2)	85 (8.5)	
Single	33 (9.8)	17 (8.9)	20 (9.6)	8 (4.4)	1 (1.2)	79 (7.9)	
Widowed	18 (5.3)	8 (4.2)	8 (3.8)	13 (7.2)	5 (6.0)	52 (5.2)	
<i>Occupational status, n (%)</i>							$p < 0.001^*$
Employed	118 (34.9)	71 (37.4)	82 (39.2)	45 (25.0)	26 (31.3)	342 (34.2)	
Self-employed	36 (10.7)	14 (7.4)	20 (9.6)	12 (6.7)	6 (7.2)	88 (9.6)	
Housewife	78 (23.1)	41 (21.6)	57 (27.3)	73 (40.6)	29 (34.9)	278 (27.8)	
Unemployed	34 (10.1)	14 (7.4)	25 (12.0)	25 (13.9)	10 (12.0)	108 (10.8)	
Unable to work	2 (0.6)	0	1 (0.5)	1 (0.6)	0	4 (0.4)	
Retired	70 (20.7)	50 (26.3)	24 (11.5)	24 (13.3)	12 (14.5)	180 (18.0)	
<i>Education, n (%)</i>							$p = 0.001^*$
No formal education	1 (0.3)	3 (1.6)	3 (1.4)	0 (0.0)	2 (2.4)	9 (0.9)	
Bachelor's degree or higher	55 (16.3)	34 (17.9)	45 (21.5)	40 (22.2)	18 (21.7)	192 (19.2)	
Other	282 (83.4)	153 (80.5)	161 (77.0)	140 (77.8)	63 (75.9)	799 (79.9)	
<i>Number of children, n (%)</i>							$p < 0.001^*$
0	75 (22.2)	35 (18.4)	45 (21.5)	22 (12.2)	9 (10.8)	186 (18.6)	
1	118 (34.9)	63 (33.2)	54 (25.8)	38 (21.1)	14 (16.9)	287 (28.7)	
2	110 (32.5)	66 (34.7)	85 (40.7)	83 (46.1)	42 (50.6)	386 (38.6)	
3	30 (8.9)	20 (10.5)	16 (7.7)	31 (17.2)	13 (15.7)	110 (11.0)	
4+	5 (1.5)	6 (3.2)	9 (4.3)	6 (3.3)	5 (6.0)	31 (3.1)	
<i>Children living at home, n (%)</i>							$p = 0.001^*$
0	174 (51.5)	98 (51.6)	92 (44.0)	62 (34.4)	30 (36.1)	456 (45.6)	
1+	164 (48.5)	92 (48.4)	117 (56.0)	118 (65.6)	53 (63.9)	544 (54.4)	
Total	338	190	209	180	83	1000	

Percentages denote the proportion of participants in each category for that particular geographical region.

\* $p < 0.05$ .

Participants were further asked which of their VVA and other menopausal symptoms they believed were a direct cause of the menopause. Of the 1000 participants, 733 attributed hot flushes to the menopause and 678 attributed vaginal/vulvar dryness to it. For vaginal/vulvar dryness, the rate ranged from 55.4% (Islands) to 76.1% (Central) ( $p = 0.003$ ) (Figure 2). Significant regional differences were also observed for depression (range 26.8% [Central] to 45.8% [Islands],  $p = 0.018$ ) and breast pain/tenderness (range 3.0% [North-West] to 10.0% [South],  $p = 0.006$ ).

### Impact of VVA on sexual activity and other aspects of life

VVA negatively affected the sex lives of the Italian REVIVE participants. Notably, vaginal/vulvar dryness had affected sexual activity in the previous 12 months in just over half (50.6%) of the 1000 participants. Pain during intercourse had affected sexual activity in the previous 12 months in 20.5% of participants and vaginal/vulvar irritation had affected it in 15.6% of participants. For the effects of different VVA symptoms on sexual activity, there were no significant differences between different geographical regions ( $p = 0.258$ , Pearson's chi-squared test). Importantly, two-fifths of the participants ( $n = 397$ ) did not agree that they could live with the loss of intimacy caused by their VVA symptoms, while VVA symptoms prevented 52.1% of participants from being as sexually spontaneous as they would like. There were no regional differences for loss of intimacy ( $p = 0.391$ ) or sexual spontaneity ( $p = 0.148$ ). Over one-third of participants (37.3%) reported making excuses not to have sex because of their VVA symptoms, with no regional differences ( $p = 0.724$ ).

VVA symptoms also affected other aspects of the participants' lives, interfering with sleep in 30.3% of participants, the relationship with their partner in 66.0% of participants, and enjoyment of life in general in 40.7% of participants. There were no significant regional differences ( $p > 0.05$ ).

### Health care for VVA

Participants were asked how many times during the previous 12 months they had visited their primary HCP for gynecological reasons. Of the 961 participants who answered this question, 276 (28.7%) had made no such visits to HCP; 457 (47.6%) had made one visit and 147 (15.3%) two visits. Only 81 of the respondents (8.4%) had made three or more visits to their HCP for gynecological reasons. While there was some evidence of regional variation – 24.0% of respondents in the South had made no visits compared to 32.1% for the Islands, 13.1% of participants in Central Italy had made three or more visits versus 4.9% in the North-East – overall there were no significant geographical differences ( $p = 0.063$ , Pearson's chi-squared test).

When asked whether they had ever discussed any of their VVA symptoms with a HCP, two-thirds of the participants ( $n = 666$ ) reported that they had done so; 219 had never done so and 115 could not remember or were unsure. While there was modest regional variation in the proportion of participants who had never discussed their VVA symptoms with a HCP (range 18.3% [North-West] to 27.2% [South]), there were no significant differences ( $p = 0.341$ ). The participants who had discussed their VVA

Figure 1. VVA symptoms and diagnoses by geographical region. A: Proportions of participants reporting individual VVA symptoms after the menopause. B: Proportions of participants ever diagnosed with VVA.  $p$  values is for Pearson's chi-squared test.

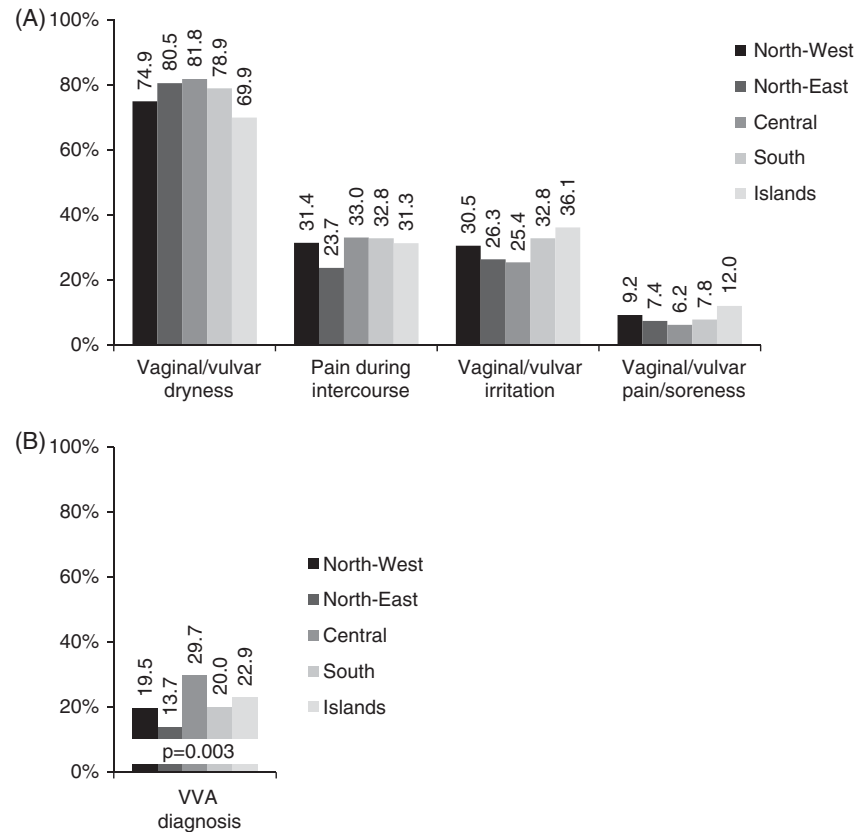
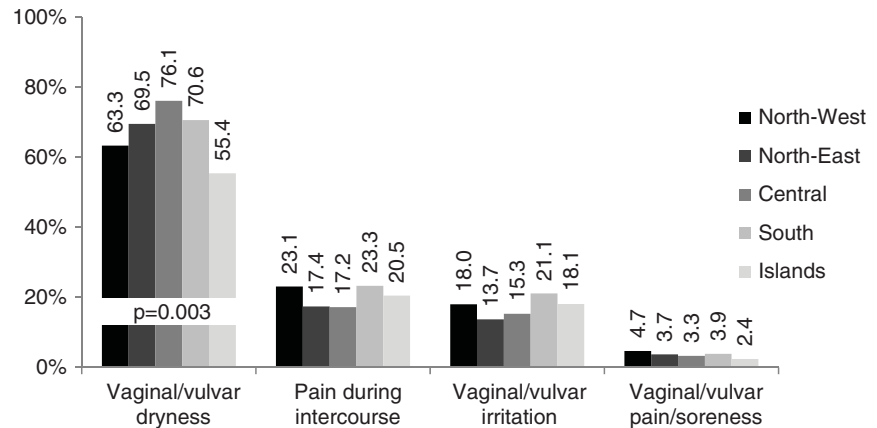


Figure 2. Proportions of women attributing their VVA symptoms to the menopause by geographical region.  $p$  values is for Pearson's chi-squared test.



symptoms with a HCP were asked who had initiated the first discussion. Of the 665 participants who answered this question, 563 (84.7%) had initiated the discussion themselves – either during a checkup or by specifically booking an appointment to discuss their symptoms. There were no significant regional differences ( $p=0.136$ ).

### VVA treatments

Participants were asked to indicate which treatments they had ever used for their VVA symptoms. The two most frequently used products were both OTC medications: a product range based partly on hyaluronic acid (used at some point by 50.5% of participants) and a plant extract-based cream (23.8%).

There were significant geographical differences in lifetime use of VVA treatments ( $p=0.003$ , Pearson's chi-squared test). Notably, one particular OTC medication based on hyaluronic

acid was more frequently used on the Islands (9.6%) than in other regions (1.4 to 2.2%) ( $p<0.001$ ). Prescription medications based on testosterone cream compounded at pharmacies were more frequently used in North-East Italy (2.1%) compared to other regions (0.0 to 0.6%) ( $p=0.011$ ), although few participants were using testosterone. Geographical differences for other VVA treatments were not statistically significant.

There were no overall geographical differences in current use of different VVA treatments ( $p=0.208$ ). The above-mentioned OTC product range was the treatment that was currently being used by the highest number of participants ( $n=264$ ).

A total of 698 participants reported having ever used one or more of 11 listed OTC medications for VVA, with the proportion varying from 63.6% in Central Italy to 74.2% in the North-East. Reported use of natural products ranged from 7.1% in the North-West to 8.9% in the North-East. Prescription medications for VVA (estrogen and testosterone) showed more marked regional trends,

with 10.5% of women in Central Italy having used them compared to 5.0% in the South. Very few women had ever used a medical device to treat their VVA symptoms.

Current use of VVA treatments mirrored lifetime use. OTC medications (range 40.2% in Central Italy to 51.6% in the North-East) were more commonly used than other treatments. Current use of natural products (2.4% in Central Italy and on the Islands to 5.3% in the North-East) and prescription medications (1.2% on the Islands to 5.7% in Central Italy) showed evidence of regional variation. Only one woman was currently using testosterone and none were using a medical device.

## Discussion

This analysis of Italian data from the wider European REVIVE study reveals regional differences in VVA symptoms and their treatment. Notably, the rate of VVA diagnosis was higher in Central Italy than in the North-East. The proportion of participants who had made three or more health-care visits for gynecological reasons in the previous 12 months was more than twice as high in Central versus North-East Italy (13.1% versus 4.9%). However, the difference in VVA diagnosis rate did not reflect a *significant* difference between these two regions in either number of health-care visits or likelihood of having discussed VVA symptoms with a HCP. A recent analysis of data for the year 2006 from an annual international survey – European Union Statistics on Income and Living Conditions (EU-SILC) – found that unmet medical needs due to unavailability of health care (long waiting lists) were more frequent in Central Italy (25.1%) compared to the North-East (16.7%) [17]. This suggests that the higher rate of VVA diagnosis in Central versus North-East Italy in the present study is not due to a difference in health-care availability.

The proportion of participants who had never discussed their VVA symptoms with a HCP was highest in the South of Italy. While an exploration of reasons why participants had not discussed their VVA symptoms with a HCP revealed no significant regional differences (data not shown), there is evidence that health care is inferior in terms of quality or coverage in South Italy compared to other regions of the country [18]. According to the 2006 EU-SILC data [17], the proportion of adults with unmet medical needs was higher in the South (10.6%) than in the North-East (4.6%) and North-West (4.9%). Per capita health-care expenditure is generally higher in the North than in Central Italy and the South [19], and survey data from 1993 and 2005 suggest that the perceived quality of public health services is lower in the South than in Central Italy and the North [20]. This is in spite of (or perhaps a contributor to) higher rates of obesity, sedentary behavior, and hospitalization in the South than in other parts of Italy [16,18]. Deficiencies in health care in the South have been attributed mainly to cultural factors [17,20]. One or more of these cultural elements may explain the relatively high proportion of women in South Italy who had never discussed their VVA symptoms with a HCP [21]. Additionally, we cannot exclude specific socio-cultural attitudes of both women and HCPs toward discussing intimate topics [22], which could be related with a higher ratio of male gynecologists in the South.

There were regional differences in the percentages of participants attributing vaginal/vulvar dryness and other menopausal symptoms to the menopause. A plausible explanation for these differences is regional differences in health education or the provision of information about the menopause. Previous studies of knowledge of the menopause among Italian women did not specifically examine the role of geography [16,23,24].

Observed geographical differences in the use of certain medications may be explained by a number of factors. Starting in the 1970s and gathering pace since the 1990s, Italian health

care has undergone a process of decentralization, which has contributed to considerable regional differences in the use of certain medications [25]. Moreover, there is evidence of regional differences in the public funding of medications in favor of poorer regions such as those in the South [26]. In spite of this, reported use of prescription medications in the present study was actually lower in women in Southern Italy than in women living in other regions of the country.

Some of the findings in the present study may be attributed to previously documented socio-cultural differences between northern and southern regions of Italy [27]. Others may be partly explained by the observed inter-regional differences in demographics: age, marital status, occupational status, education, number of children, and having children living at home. Marital status, occupational status, and education were previously identified as key predictors of self-rated health in the Italian population [19]. In the context of VVA, age in particular may be important, given that 25.4–41.6% of Italian REVIVE participants reported that their symptoms were worse at the time of the survey compared to when they first arose.

The current study has limitations and strengths. The present findings may have been affected by the biases that typically affect surveys, such as recall bias and response bias. Also, multiple statistical comparisons were conducted without multiple testing correction, which means that some of the significant findings are potentially a result of chance. Moreover, because the study explored differences between five geographical regions in one of the four countries included in the European REVIVE study, numbers of participants were modest compared to the overall European REVIVE sample ( $n = 3768$ ). Nonetheless, the geographical subgroups were representative of the population distribution of Italy. Additionally, this is a nation-wide multicenter research that investigates VVA among women eventually attending gynecological services and that depicts a real-world situation of the Italian clinical practice. Moreover, the survey questionnaire was initially tested in a subset of participants to make sure that the questions could be understood.

## Conclusions

The present analyses reveal modest differences in knowledge, diagnosis, and treatment of VVA between different Italian regions. Published literature on inter-regional differences in health care in Italy provides potential explanations for some of the present findings. The challenge remains to ensure that all menopausal women in Italy are properly informed about VVA and have adequate access to the necessary health care and treatments. Multivariate logistic regression of the above-mentioned EU-SILC data showed that the odds of unmet medical needs were significantly higher in women compared to men [17]. The odds of unmet medical needs specifically attributable to inaccessibility of health care (itself largely due to the costs involved) were also higher in women. In Tuscany (Central Italy), an ongoing collaboration involving clinicians, HCPs, and policy-makers seeks to reduce geographic variation in health care that is not justified based on the needs of patients [28]. Extension of this approach to the macro-regional and national levels and its specific application to VVA may be warranted.

## Acknowledgements

The authors would like to thank Emili González-Pérez and Stephen Gilliver (TFS Develop) for their assistance with manuscript preparation. Sponsorship and article processing charges for this study were funded by Shionogi, Inc.

## Declaration of interest

Rossella E. Nappi has a financial relationship (lecturer, member of advisory boards, and/or consultant) with Bayer HealthCare AG, Endoceutics, Gedeon Richter, HRA Pharma, Merck Sharpe & Dohme, Novo Nordisk, Pfizer Inc, Shionogi Limited, TEVA Women's Health Inc.

Martire Particco is employee of Shionogi Italy.

Nicoletta Biglia has a financial relationship (lecturer, member of advisory boards and/or consultant) with Gedeon Richter, Shionogi Limited, Merck Sharpe & Dohme, and Italfarmaco SpA.

Costantino Di Carlo has a financial relationship (lecturer, member of advisory boards and/or consultant) with Bayer HealthCare AG, Gedeon Richter, HRA Pharma, Merck Sharpe & Dohme, Shionogi Limited and TEVA Women's Health Inc.

The other authors have no conflicts of interest.

This work was supported by Shionogi, Inc.

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