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Remission, Relapse, and Persistence of Vulvodynia: A Longitudinal Population-Based Study

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Abstract

Background: Vulvodynia has been considered to be a chronic disorder. We sought to estimate the probability of and risk factors for remission, relapse, and persistence among women screening positive for vulvodynia.
Methods: Survey-based assessment in a longitudinal population-based study of women (the Woman to Woman Health Study) who screened positive for vulvodynia and completed at least four follow-up surveys. Outcome measures included remission without relapse, relapse (after remission), and persistence of a positive vulvodynia screen. Multinomial regression was used to assess factors associated with outcomes.
Results: Of 441 women screening positive for vulvodynia during the study, 239 completed 4 additional surveys. Of these, 23 (9.6%) had consistently positive vulvodynia screens, 121 (50.6%) remitted without relapse, and 95 (39.7%) relapsed following remission. Overall, factors associated with both relapse and persistence (compared with remission alone) included increased severity of pain ever ($p < 0.001$) or after intercourse ($p = 0.03$), longer duration of symptoms ($p \leq 0.001$), and screening positive for fibromyalgia ($p < 0.001$). Factors associated with persistence (but not relapse) included more severe symptoms with intercourse ($p = 0.001$) and pain with oral sex ($p = 0.003$) or partner touch ($p = 0.04$). Factors associated with relapse (but not persistence) included having provoked pain ($p = 0.001$) or screening positive for interstitial cystitis ($p = 0.05$) at first positive vulvodynia screen. Demographic characteristics, age at pain onset, and whether vulvodynia was primary or secondary did not predict outcome.
Conclusion: Remission of vulvodynia symptoms is common with approximately half of remitters experiencing a relapse within 6–30 months. Persistence without remission is the exception rather than the rule. Pain history and comorbid conditions were associated with the more severe outcomes of relapse and/or persistence compared with those who remitted only. These findings provide further support that vulvodynia is heterogeneous and often occurs in an episodic pattern.

Introduction

Vulvodynia has long been understood to be a chronic condition. With a prevalence of 8.3% and an annual incidence of ~4.2% per 100 woman-years, it poses a considerable burden to women's health.[1] Until recently, it was thought that once vulvodynia developed it would persist.[2–4] A limited number of studies now have included a follow-up evaluation and have documented that not all women with vulvodynia continue to report such symptoms at follow-up, suggesting that remission does occur.[5–7] Clinical experience suggests that women who experience remission remain at high risk of relapsing symptoms. However, the rates of persistence, remission, and relapse are currently unknown, and the factors associated with these clinical trajectories have not been investigated.

Retrospective recall of symptoms suggestive of vulvodynia is likely biased as women often fail to recall prior pain documented at an earlier visit.[7] We conducted a prospective study to more accurately measure the presence and absence of symptoms suggesting vulvodynia over time and to assess the frequency of persistence, remission, and relapse in a population-based study. A population-based approach captures the breadth of vulvodynia symptoms and clinical course present in the community. We previously reported on the prevalence and incidence of vulvodynia in a population-based longitudinal study of women in southeast Michigan.[1,8] This report describes further analyses demonstrating the rates of persistence, remission, and relapse of vulvodynia among those screening positive for the disorder and risk factors associated with these clinical trajectories.

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Materials and Methods

The study was approved by the University of Michigan IRB. Methods for enrollment and sampling probabilities have been published previously.[1] In brief, a population-based sample of women aged 18 years and older living in a four-county area in southeast Michigan were enrolled by the Survey Research Operations at the Institute for Social Research at the University of Michigan Woman to Woman Health Study using random digit dialing.

After giving oral informed consent and completing a short interview, participants were sent a 26-page survey, which included a previously validated screen for vulvodynia as well as questions about women's demographic characteristics, health history, exposures, current symptoms, and other potential risk factors. The survey also included a limited set of screens for other pain and psychological conditions, including those for fibromyalgia, interstitial cystitis, irritable bowel disorder, depression, and post-traumatic stress disorder (PTSD). Those completing the baseline survey were sent additional follow-up surveys every 6 months. A small stipend, varying from $5 for the initial survey to $25 for the 36-month follow-up survey, was given to the participants. This report is based on information obtained from baseline through the 36-month follow-up survey.

Eligibility

Of the 2,542 women enrolled in the Woman to Woman Health Study, eligible women had to have completed the baseline comprehensive survey, including all questions necessary for the vulvodynia screen. Because the possibility of relapse was increasing over time, only the data for those with at least four additional surveys are presented for remission and relapse rates and factors associated with outcomes to provide a consistent yet maximum follow-up period for each included participant.

Definitions

The vulvodynia screen used was verified previously[9] and includes the current presence of pain at the opening to the vagina with or without provocation that has been present for at least 3 months and has not resolved. Remission was defined as no longer meeting criteria for vulvodynia following a positive screen. Relapse was defined as again screening positive for vulvodynia following such a remission. Persistence was defined when a woman continued to have positive vulvodynia screens at every follow-up subsequent to the initial positive screen.

The screens used for other comorbid pain and psychological conditions included the: Fibromyalgia Impact Questionnaire for fibromyalgia,[10,11] Rice High Specificity definition for interstitial cystitis,[12] Rome II criteria for irritable bowel syndrome (IBS),[13,14] PHQ-8 for depression,[15,16] and PC-PTSD for PTSD.[17]

Primary vulvodynia was defined as those who either had their vulvar pain with first intercourse or first tampon use or, if these data were incomplete, if they reported their vulvar pain began before the age of 20.

Analysis

Frequencies were assessed for all variables used in the analysis. Because the clinical outcome could change over the course of the study (with increasing numbers of women demonstrating a relapse), the clinical outcome measures of remission, relapse, and persistence were determined based on the results of the vulvodynia screens on two, three, and four surveys completed following the first positive screen. Thereafter, the analyses were conducted using the data for those with at least four surveys completed after the first positive survey to maximize the time followed and to maintain consistency in the number of follow-up surveys analyzed.

For the analyses of remission and relapse rates, Poisson regression analysis was performed using data from the time of the initial positive vulvodynia screen to calculate remission rates and from time of first remission to calculate relapse rates. Chi square analysis was used to determine the relationship between clinical outcome and whether the participant was currently taking a medication for pain or for depression.

The association between potential risk factors and the categories of remission without relapse, relapse, and persistence was assessed using multinomial logistic regression with potential risk factors, measured at the time of a first positive vulvodynia screen, included as covariates, controlling for age. Odds ratios for all pairwise comparisons of relapse versus remission, persistence versus remission, and persistence versus relapse were determined.

Results

Eligibility

Of the 2,542 women enrolled in the Woman to Woman Health Study, 267 did not complete the baseline comprehensive survey and an additional 82 did not complete all questions necessary for the vulvodynia screen—leaving a total of 2,193 potential participants for this analysis, 1,763 (80.4%) of whom were still participating at the 36-month survey. Of the 2,193 women, 441 screened positive for vulvodynia either at baseline ($n=238$) or on one of the subsequent five follow-up surveys ($n=203$). The average number of surveys completed overall for the 441 cases was 5.3 ± 1.4 (median = 6, mode = 6). Of the 441 women screening positive, 347 (78.7%) had at least two surveys completed after being categorized as a case, 302 (68.5%) completed a minimum of three surveys after the first positive survey, and 239 (54.2%) completed four surveys and were included in the analyses.

Women excluded from the analyses because of insufficient follow-up after becoming a case did not differ in age (45.6 vs. 46.3 years, $p=0.67$), ethnic/racial group (74.5% vs. 83.0% white, nonHispanic, $p=0.17$), marital status (71.0% vs. 77.7% married or living as married, $p=0.17$), household income >$60,000 (56.2% vs. 61.8%, $p=0.46$), or college graduation (52.1% vs. 55.9%, $p=0.51$) compared with women included in the analysis.

Remission, relapse, and persistence prevalence

The proportions of women who demonstrated a remission without relapse, a relapse, or persistence of a positive screen varied, depending on how many follow-up surveys were completed or considered in the analysis (Fig. 1). The remission rate was substantial (67.1% within two surveys of the initial positive survey), but over time, more than half of women who reported remission had a relapse.

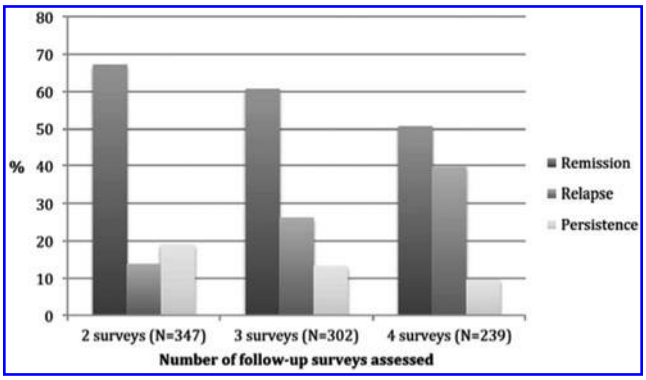

FIG. 1. Proportions with remission without relapse, relapse following remission, or persistence.

Because of the increasing proportion of women demonstrating a relapse based on the number of surveys completed, we limited the variability and maximized the time followed for each woman by limiting the further analyses to those completing four surveys after the first positive screen.

Among the 239 women with a positive screen for vulvodynia with at least four follow-up surveys completed, 121 (50.6%) had a remission without relapse, 95 (39.7%) had a remission with relapse documented, and 23 (9.6%) persisted throughout the time observed by follow-up surveys. The clinical course did not differ by demographic characteristics of the women, including age, ethnicity, or ability to pay for basics (food, shelter), although those with persistent symptoms were more likely to be married (Table 1).

Since the probability of remission soon after screening positive was high, we assessed whether remission was more likely to be observed when women became positive on a survey after the baseline survey, as opposed to when they screened positive at the baseline survey. Regardless of which survey contained the initial positive vulvodynia, we found that the majority of observed remissions occurred at the following survey (data not shown).

Table 1. Demographic Characteristics (at Study Entry) Stratified by Outcome Among Those Participants with Four or More Completed Surveys Following a Positive Vulvodynia Screen ($N=239$)

Characteristics	*Remission 121 (50.6%)*	*Relapse 95 (39.7%)*	*Persist 23 (9.6%)*	p
Age (mean ± SD in years)	47.6 ± 14.6	47.1 ± 13.6	48.2 ± 11.8	0.93
Ethnicity				0.49
White	86.8%	82.1%	78.3%	
Black	5.8%	10.5%	4.3%	
Hispanic	3.3%	2.1%	8.7%	
Other	4.1%	5.3%	8.7%	
Married or living as married	78.5%	80.9%	100.0%	0.05
Hard to pay for basics	40.2%	33.7%	34.8%	0.61

Rates of remission and relapse

Among the 239 women screening positive for vulvodynia and having four additional follow-up surveys, the average time followed was 593.3 ± 62.2 days (median 575 days), and 216 (90.3%) had a remission during that time. The remission rate adjusted for time followed until remission occurred was 88.6 cases per 100 woman-years (95% CI 77.6, 100.0) over the 3 years of the study. No difference in remission rates were noted when stratified by age or ethnicity, but the remission rate was less (82.0 cases/100 woman-years [95% CI 70.7, 95.1]) in those currently married or living as married.

Of the 216 women with a remission who completed at least one further survey, (*i.e.,* did not have their remission on the fourth survey following the first positive screen) 111 (51.3%) had subsequently relapsed, with a relapse rate over the remaining surveys of 32.4 cases per 100 woman-years (95% CI 26.9, 39.1) following remission. The rate of relapse after a remission was not associated with age, ethnicity, or marital status.

Women often denied having had symptoms that they had reported on earlier surveys. Among the 103 women who had initially reported vulvar pain and subsequently had a remission, 39 (37.9%) reported no history of vulvar pain at their follow-up visit. However, the probability a woman would screen positive again (relapse) on a subsequent survey versus reporting no further vulvar symptoms was equally likely whether the participant had confirmed her previously reported vulvar pain (46.9%) or not (41.0%, $p=0.68$).

Factors associated with vulvodynia remission, relapse, or persistence

The relationship between potential factors associated with remission, relapse, and persistence was assessed using multinomial regression, controlling for age. Women with remission, relapse, or persistence did not differ by health rating, rating of physical pain in general, or general pain interference as reported at the time of the first positive vulvodynia screen ($p>0.05$, data not shown). However, prognosis was associated with a number of factors (Table 2).

If the pain was described as provoked, women had increased odds of having recurrent vulvodynia and were less likely to remit. Both pain with intercourse and pain after intercourse were associated with relapse and persistence. Pain with oral sex, masturbation, and having an orgasm were not commonly reported; however, those with pain with oral sex or with partner touch were more likely to persist. The more severe the rating of the worst pain ever and the longer the pain had been present were associated with greater odds of relapse and persistence. However, neither the age at onset of pain nor whether the pain was primary or secondary was associated with relapse or persistence. Pain quality (sharp, stabbing, burning, or itching) was not associated with prognosis (data not shown).

Comorbid pain conditions are known to be associated with vulvodynia,[18–21] and in fact, the presence of fibromyalgia and interstitial cystitis, but not IBS, at the time of first positive vulvodynia screen was associated with the increased odds of persistence compared with either remission or relapse. Similarly, screening positive for depression, but not for PTSD, at the time of first positive vulvodynia screen was associated with more persistent vulvodynia than if the screen was negative.

Table 2. Risk Factors for Various Clinical Courses (Remission, Relapse, and Persistence) After Screening Positive for Vulvodynia (Adjusted for Age; $N=239$)

Risk factors	*Frequency at first positive screen*	*Frequencies within each outcome group*				*Pairwise comparison of likelihood of group membership by risk factor*[b]		
		Remission, n *(%)*	*Relapse,* n *(%)*	*Persistent,* n *(%)*	p[a]	*Relapse vs. remission OR (95% CI)*	*Persistent vs. remission OR (95% CI)*	*Persistent vs. relapse OR (95% CI)*
Pain characteristics								
Provoked vulvar pain versus not ($n=229$)	193 (84.3)	87 (76.3)	84 (91.3)	22 (95.7)	**0.001**	**3.34 (1.43, 7.82)**	6.75 (0.86, 52.74)	2.02 (0.24, 17.11)
Spontaneous vulvar pain versus not ($n=217$)	58 (26.7)	33 (30.3)	20 (22.7)	5 (25.0)	0.484	0.68 (0.36, 1.29)	0.75 (0.25, 2.25)	1.11 (0.36, 3.44)
Pain with intercourse ($n=236$)					0.074			
None	92 (39.0)	56 (46.7)	33 (34.7)	3 (14.3)		Reference	Reference	Reference
Mild	87 (36.9)	42 (35.0)	36 (37.9)	9 (42.9)		1.46 (0.78, 2.70)	**3.99 (1.02, 15.66)**	2.74 (0.68, 11.01)
Moderate	39 (16.5)	14 (11.7)	19 (20.0)	6 (28.6)		**2.32 (1.03, 5.24)**	**7.86 (1.74, 35.47)**	3.39 (0.76, 15.18)
Severe	18 (7.6)	8 (6.7)	7 (7.4)	3 (14.3)		1.49 (0.50, 4.50)	**6.93 (1.19, 40.44)**	4.64 (0.77, 28.01)
Pain after intercourse ($n=236$)					**0.032**			
None	130 (55.1)	87 (55.8)	54 (56.8)	9 (42.9)		Reference	Reference	Reference
Mild	75 (31.8)	45 (37.5)	23 (24.2)	7 (33.3)		0.63 (0.34, 1.18)	1.20 (0.42, 3.47)	1.90 (0.63, 5.73)
Moderate	24 (10.2)	6 (5.0)	15 (15.8)	3 (14.3)		**3.10 (1.20, 8.56)**	3.99 (0.84, 19.01)	1.29 (0.31, 5.42)
Severe	7 (3.0)	2 (1.7)	3 (3.2)	2 (9.5)		1.86 (0.30, 11.57)	**8.27 (1.01, 67.58)**	4.46 (0.64, 31.20)
Sexual activities causing pain ($n=233$)								
Oral sex	19 (8.2)	7 (6.0)	6 (6.4)	6 (27.3)	**0.003**	1.06 (0.35, 3.29)	**5.98 (1.78, 20.11)**	**5.61 (1.60, 19.68)**
Masturbation	10 (4.3)	6 (5.1)	4 (4.3)	0 (0)	0.553	0.84 (0.23, 3.11)	—	—
Having an orgasm	7 (3.0)	4 (3.4)	0 (0)	3 (13.6)	**0.003**	—	4.69 (0.95, 23.17)	—
Partner touch to area	59 (25.3)	24 (20.5)	25 (26.6)	10 (45.5)	**0.044**	1.41 (0.74, 2.67)	**3.22 (1.24, 8.35)**	2.29 (0.88, 5.96)
Severity of pain ($n=211$)								
Impact on intercourse								
Discomfort	168 (79.6)	85 (83.3)	68 (78.2)	15 (68.2)	0.100	Reference	Reference	Reference
Frequently prevented intercourse	31 (14.7)	9 (8.8)	16 (18.4)	6 (27.3)		2.22 (0.92, 5.33)	**3.79 (1.18, 12.21)**	1.71 (0.57, 5.10)
Impossible to have intercourse	12 (5.7)	8 (7.8)	3 (3.4)	1 (4.5)		0.49 (0.12, 1.93)	0.68 (0.08, 5.93)	1.39 (0.13, 14.59)
Worse vulvar pain ever (rated 0–10 excruciating; mean ± SD) ($n=232$)	5.3 ± 2.9	4.6 ± 2.8	5.9 ± 2.8	6.4 ± 2.4	**0.001**	**1.18 (1.06, 1.30)**	**1.26 (1.06, 1.49)**	1.07 (0.90, 1.27)

(*continued*)

TABLE 2. (CONTINUED)

Risk factors	*Frequency at first positive screen*	*Frequencies within each outcome group*				*Pairwise comparison of likelihood of group membership by risk factor*[b]		
		Remission, n *(%)*	*Relapse,* n *(%)*	*Persistent,* n *(%)*	p[a]	*Relapse vs. remission OR (95% CI)*	*Persistent vs. remission OR (95% CI)*	*Persistent vs. relapse OR (95% CI)*
Duration of pain								
Years of reported vulvar pain at time of positive screen (mean ± SD) (*n* = 237)	11.6 ± 12.6	9.7 ± 11.9	13.3 ± 13.1	15.0 ± 12.2	**<0.001**	**1.03 (1.01, 1.05)**	**1.04 (1.00, 1.07)**	1.01 (0.97, 1.04)
Years of reported vulvar pain in quartiles (*n* = 237)								
0–2 years	62 (26.2)	40 (33.3)	16 (17.0)	6 (26.1)	**0.006**	Reference	Reference	Reference
2–5.5 years	44 (18.6)	22 (18.3)	22 (23.4)	0 (0)		**2.53 (1.10, 5.80)**	—	—
5.5–15 years	66 (27.8)	32 (26.7)	27 (28.7)	7 (30.4)		2.08 (0.96, 4.52)	1.45 (0.44, 4.74)	0.70 (0.20, 2.44)
>15 years	65 (27.4)	26 (21.7)	29 (30.9)	10 (43.5)		**3.00 (1.35, 6.69)**	2.67 (0.84, 8.48)	0.89 (0.26, 2.99)
Age at first pain with intercourse (years; *n* = 194)	33.4 ± 14.8	34.9 ± 15.4	31.9 ± 13.9	33.5 ± 15.4	0.419	0.98 (0.96, 1.01)	0.99 (0.95, 1.03)	1.01 (0.97, 1.05)
Primary vulvodynia (*n* = 238)	102 (42.9)	50 (41.3)	44 (46.8)	8 (34.8)	0.515	1.24 (0.72, 2.13)	0.76 (0.30, 1.94)	0.62 (0.24, 1.60)
Comorbid pain conditions								
Screened positive at time of first positive vulvodynia screen (*n* = 239)								
Fibromyalgia	42 (17.6)	11 (9.1)	20 (21.1)	11 (47.8)	**<0.001**	**2.70 (1.22, 5.96)**	**9.21 (3.29, 25.80)**	**3.42 (1.31, 8.92)**
Interstitial cystitis	33 (14.0)	11 (9.1)	16 (17.3)	6 (26.1)	**0.047**	2.09 (0.92, 4.75)	**3.59 (1.17, 11.04)**	1.72 (0.58, 5.07)
Irritable bowel disorder	41 (17.2)	18 (14.9)	17 (17.9)	6 (26.1)	0.413	1.23 (0.59, 2.57)	2.09 (0.72, 6.10)	1.69 (0.57, 5.01)
Comorbid psychological disorders								
Screened positive for depression at time of first positive vulvodynia screen (*n* = 237)	45 (19.0)	19 (15.7)	18 (19.4)	8 (34.8)	0.101	1.28 (0.62, 2.61)	**2.99 (1.10, 8.17)**	2.35 (0.85, 6.50)
Screened positive for PTSD at time of first positive vulvodynia screen (*n* = 236)	38 (16.1)	19 (15.7)	13 (14.1)	6 (26.1)	0.372	0.86 (0.40, 1.86)	1.96 (0.67, 5.70)	2.28 (0.75, 6.98)

The entries marked by "—" are not reported due to very low number of participants, resulting in an unstable finding.
Statistically significant findings are bolded for clarity.
[a]*p*-Value based on analysis of variance or chi square analysis of differences in frequencies of the factors among those with remission, relapse, and persistence.
[b]Controlled for age.
PTSD, post-traumatic stress disorder.

To assess whether restriction of analyses to women with four follow-up visits biased study results, we reran analyses based on having at least two and at least three follow-up visits (which limits the opportunity for a relapse to be observed). Results using these data did not differ substantively from those presented here (data not shown).

Association with current treatment and outcome

Rarely have studies assessing remission reported on current medications being taken by those reporting symptoms or lack of symptoms. We assessed whether the participants reported taking medication at the time of first positive screen or at the time of first remission that might alter vulvar pain. These included those used for pain or the neurotransmitter-altering drugs commonly used for psychological issues.

Clinical outcome was not associated with use of medications for pain or neurotransmitter-altering drugs ($p > 0.29$). In addition, when asked whether they were on a treatment for the vulvar pain, only 30 (12.5%) reported taking medications (or combinations of two medications) at the time of their first positive screen. Reported treatments included estrogen ± progesterone in 50.0% (15/30), antifungals in 13.3% (4/30), topical steroids in 20.0% (6/30), topical cream or moisturizer in 23.3% (7/30), and miscellaneous treatments in 13.3% (4/30). None were on antidepressants, pain medication, or anticonvulsants for their vulvar pain.

Discussion

This is one of the first longitudinal population-based studies to prospectively determine probabilities of remission, relapse, and persistence among women screening positive for vulvodynia. We found the probability of remission was quite high, but approximately half of those whose symptoms resolved had a relapse of symptoms within a short period of time. Persistence of symptoms at every screening was only present in ~10% of those with a positive survey who were followed for at least four additional surveys.

Vulvodynia has traditionally been considered to be a chronic disorder, with little recognition of remissions or relapse. Peckham was one of the first to report remission after a woman was diagnosed with having vulvodynia: over 15 years, 50% of his 67 cases reported no further symptoms, with most remissions occurring in the first 6 months after diagnosis.[22] Furthermore, studies assessing nonclinic-based populations suggest that a substantial proportion of women who report past vulvodynia deny ongoing symptoms.[1,6,23,24] Cross-sectional surveys conducted online,[25] in a population-based survey conducted in the Boston area,[23] and in the initial survey of this longitudinal population-based study of vulvodynia[1] estimated that 16%–27.9% of the populations had met survey-based criteria for vulvodynia at some point, but only 1.7%–8.3% reported current symptoms, suggesting remission could occur in a substantial proportion of sufferers.

Sutton et al. reported a remission rate of 31.4% at a 1-year follow-up, but if all those who had met criteria for vulvodynia at the initial screen who denied symptoms at the 1-year follow-up were included in the analysis, a remission rate of 66.7% (48/72 women) would be seen.[7] Nguyen et al. questioned women with screened and verified vulvodynia about periods in the past in which vulvar pain resolved (remission) and reported an overall remission rate of 33.0% (46/138).[26] However, by design, all women in their study had vulvar pain consistent with vulvodynia and hence all with a remission had subsequently relapsed, whereby those without a relapse would not have been within their study population. More recently, Davis et al. found that when assessing response to treatment for vulvodynia over a 2-year period, women tended to report less pain within this time frame independent of treatment used (physical therapy, medical or surgical treatment, acupuncture, *etc.*) or if no treatment was used at all, although none were reported to have gone into remission.[27]

Inconsistent reporting of the history of vulvar symptoms, in which previously reported symptoms were later denied and/or forgotten, has been noted in two prospective studies of vulvodynia and was again confirmed in the current study. In one of the first prospective assessments of vulvodynia remission, Reed et al. reported a 22.2% remission rate over 2 years among women identified from a Women's Health Registry, 60% of whom denied previous symptoms consistent with vulvodynia, despite having screened positive (with a subset validated clinically) 2 years previously.[6] Similarly, in a nationwide population-based study, Sutton et al. found that 37 of 72 women meeting criteria for vulvodynia at their baseline survey denied ever having had these symptoms when asked a year later (51.4%).[7] We considered women with symptoms that resolved to have remitted in our analysis—even when they reported no previous symptoms, while Sutton et al. excluded these women from their analysis, thereby explaining the lower remission rate (31.4%) they reported.

Some women who report resolution of vulvodynia symptoms may be taking medications for other disorders (*e.g.,* depression, anxiety, fibromyalgia, or interstitial cystitis) that may impact their vulvar neuropathic pain symptoms in some patients.[28–31] We found that very few women were being treated for their vulvar pain, with the most likely treatment being topical estrogen ± progesterone. Treatments were not associated with remission or relapse. However, no one reported treatment with the two classes of medications often used for neuropathic pain—antidepressants and anticonvulsants—and hence no conclusions can be drawn regarding the impact these medications might have on remission/relapse.[30,31]

Relapse in vulvodynia

Previous studies have not had the prospective data needed to report on the likelihood of relapse. We have demonstrated that although remission of symptoms to a level no longer meeting criteria for vulvodynia is quite common, relapse of symptoms within a short time period occurs in roughly half of these cases. With even longer follow-up, relapse rates may further increase from that demonstrated in this study.

Risk factors for remission, relapse, or persistence

The Woman to Woman Health Study reported here indicated a number of factors associated with worsening vulvodynia outcomes (relapse and/or persistence), including the presence of provoked pain, more severe pain with or after intercourse, pain with oral sex or partner touch, higher rating of worse pain ever, longer duration of pain, or screening positive for fibromyalgia, interstitial cystitis, or depression, thereby confirming, in a population-based study, some of the previously predicted findings and increasing our understanding of the relationship with comorbid conditions with vulvodynia.

Little has been written about factors associated with remission of symptoms. We had previously reported on factors associated with remission in a study of women in a Women's Health Registry and found that increased severity of past vulvar pain,[5,6] longer duration of symptoms,[5] and the presence of pain after intercourse[6] are associated with less improvement over time, consistent with our current findings. Nguyen et al. assessed reports by participants with vulvodynia in a community-based study about previous periods of no vulvar pain and found that those with primary vulvodynia were less likely to report a remission than were those with secondary vulvodynia, as were those who were either underweight or obese.[26] Those with a longer duration of symptoms were more likely to have a remission. We, however, found that a longer duration of symptoms was associated with greater relapse and greater persistence, and observed no relationship between primary versus secondary vulvodynia and prognosis.

There are two reasons these results might vary. Based on the study design, the results of Nguyen et al. reflect remission among women who have subsequently undergone a relapse—thereby not including characteristics of those who had a remission without relapse. In addition, their definition of primary vulvodynia reflected that the woman agreed that she always had pain on contact. However, if she always had such pain, it would be consistent with not having had remissions—a bias that might exist in that study. We defined primary vulvodynia as whether the woman had had pain at the vulva with first intercourse and/or first tampon use or, if missing data, if her pain started before age 20, without a stipulation that the pain has not remitted at times since onset.

Demographic characteristics, such as age, ethnicity, and education, were not associated with vulvodynia course, despite the fact that vulvodynia prevalence and incidence differ somewhat by age and ethnicity.[1,8] Further work is needed to clarify whether these differences in risk of disease, yet lack of difference in clinical course following onset, can be demonstrated to reflect differing physiology or whether they may be related to reporting bias or other unmeasured factors.

Strengths and limitations of the study

The natural history of vulvodynia in the general population can be estimated with less recall bias in a longitudinal population-based cohort—a major strength of this study. The use of a validated instrument to predict vulvodynia and the collection of a substantial number of demographic and potential risk factors over time are similarly strengths. Although the screening tool used for the vulvodynia diagnosis has been previously validated,[9] the women diagnosed with and without having vulvodynia were not clinically confirmed, and hence the diagnosis made may differ from that made in the office setting. In addition, women were not questioned regarding the denial of vulvar pain symptoms some had previously reported. Further study regarding the reasons for these inconsistencies will add to our understanding of the interpretation and meaning of this finding.

The population studied was a population-based sample of women and hence may not reflect the subset of women who seek care in the office setting—hence the remission/relapse/persistence rates may differ in a clinical subset, and further study of women seeking care is needed. Participants received a token stipend for participation at each survey to encourage retention, but loss to follow-up did occur. Nonetheless, 80.4% of those completing the initial survey were still participating by the 36-month survey. We were also limited in the evaluation of factors associated with persistence due to the smaller number of women with this outcome. Continued identification of new cases and their clinical outcomes would increase the power of the study to assess these factors.

Conclusions

In summary, remission of symptoms following vulvodynia diagnosis by a survey-based screening test of a population-based cohort is very common, but approximately half of those with remission proceed to relapse within a short period of time. Consistent reporting of vulvodynia symptoms (persistence) only occurs in the minority of those screening positive. Factors associated with outcome include several characteristics of the pain, its duration, and associated comorbid conditions, but not demographic characteristics.

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References

1. Reed BD, Harlow SD, Sen A, et al. Prevalence and demographic characteristics of vulvodynia in a population-based sample. Am J Obstet Gynecol 2012;206:170.e1–e9.
2. McKay M, Frankman O, Horowitz BJ, et al. Vulvar vestibulitis and vestibular papillomatosis. Report of the ISSVD Committee on vulvodynia. J Reprod Med 1991;36:413–415.
3. Bachmann GA, Rosen R, Pinn VW, et al. Vulvodynia: A state-of-the-art consensus on definitions, diagnosis and management. J Reprod Med 2006;51:447–456.
4. Haefner HK, Collins ME, Davis GD, et al. The vulvodynia guideline. J Low Genit Tract Dis 2005;9:40–51.
5. Reed BD, Haefner HK, Cantor L. Vulvodynia (*Vulvar dysesthesia*)—A follow-up study. J Reprod Med 2003;48: 409–416.
6. Reed BD, Haefner HK, Sen A, Gorenflo DW. Vulvodynia incidence and remission rates among adult women: A 2-year follow-up study. Obstet Gynecol 2008;112:231–237.
7. Sutton JT, Bachmann GA, Arnold LD, Rhoads GG, Rosen RC. Assessment of vulvodynia symptoms in a sample of U.S. women: A follow-up national incidence survey. J Womens Health (Larchmt) 2008;17:1285–1292.
8. Reed BD, Legocki LJ, Plegue MA, Sen A, Haefner HK, Harlow SD. Factors associated with vulvodynia incidence. Obstet Gynecol 2014;123:225–231.
9. Reed BD, Haefner HK, Harlow SD, Gorenflo DW, Sen A. Reliability and validity of self-reported symptoms for predicting vulvodynia. Obstet Gynecol 2006;108:906–913.
10. Burckhardt CS, Clark SR, Bennett RM. The fibromyalgia impact questionnaire: Development and validation. J Rheumatol 1991;18:728–733.
11. White KP, Harth M, Speechley M, Ostbye T. Testing an instrument to screen for fibromyalgia syndrome in general population studies: The London Fibromyalgia Epidemiology

Study Screening Questionnaire. J Rheumatol 1999;26: 880–884.
12. Berry SH, Bogart LM, Pham C, et al. Development, validation and testing of an epidemiological case definition of interstitial cystitis/painful bladder syndrome. J Urol 2010; 183:1848–1852.
13. Drossman DA. Irritable bowel syndrome. Gastroenterologist 1994;2:315–326.
14. Thompson WG, Creed F, Drossman DA, Heaton KW, Mazzacca G. Functional bowel disease and functional abdominal pain. Gastroenterol Int 1992;5:75–91.
15. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. J Gen Intern Med 2001;16:606–613.
16. Kroenke K, Spitzer RL. The PHQ-9: A new depression diagnostic and severity measure. Psychiatr Ann 2002;32: 509–515.
17. Prins A, Ouimette P, Kimerling R, et al. The primary care PTSD screen (PCPTSD): Development and operating characteristics. Prim Care Psychiatry 2003;9:9–14.
18. Reed BD, Harlow SD, Sen A, Edwards RM, Chen D, Haefner HK. Relationship between vulvodynia and chronic comorbid pain conditions. Obstet Gynecol 2012;120:145–151.
19. Arnold LD, Bachmann GA, Rosen R, Kelly S, Rhoads GG. Vulvodynia: Characteristics and associations with comorbidities and quality of life. Obstet Gynecol 2006;107:617–624.
20. Gardella B, Porru D, Nappi RE, Dacco MD, Chiesa A, Spinillo A. Interstitial cystitis is associated with vulvodynia and sexual dysfunction—A case-control study. J Sex Med 2011;8:1726–1734.
21. Nguyen RH, Veasley C, Smolenski D. Latent class analysis of comorbidity patterns among women with generalized and localized vulvodynia: Preliminary findings. J Pain Res 2013;6:303–309.
22. Peckham BM, Maki DG, Patterson JJ, Hafez GR. Focal vulvitis: A characteristic syndrome and cause of dyspareunia. Features, natural history, and management. Am J Obstet Gynecol 1986;154:855–864.
23. Harlow BL, Stewart EG. A population-based assessment of chronic unexplained vulvar pain: Have we underestimated the prevalence of vulvodynia? J Am Med Womens Assoc 2003;58:82–88.
24. Arnold LD, Bachmann GA, Rosen R, Rhoads GG. Assessment of vulvodynia symptoms in a sample of US women: A prevalence survey with a nested case control study. Am J Obstet Gynecol 2007;196:128.e1–e6.
25. Reed BD, Crawford S, Couper M, Cave C, Haefner HK. Pain at the vulvar vestibule: A web-based survey. J Low Genit Tract Dis 2004;8:48–57.
26. Nguyen RH, Mathur C, Wynings EM, Williams DA, Harlow BL. Remission of vulvar pain among women with primary vulvodynia. J Low Genit Tract Dis 2015;19:62–67.
27. Davis SN, Bergeron S, Binik YM, Lambert B. Women with provoked vestibulodynia experience clinically significant reductions in pain regardless of treatment: Results from a 2-year follow-up study. J Sex Med 2013;10:3080–3087.
28. Spoelstra SK, Borg C, Weijmar Schultz WC. Anticonvulsant pharmacotherapy for generalized and localized vulvodynia: A critical review of the literature. J Psychosom Obstet Gynaecol 2013;34:133–138.
29. Nunns D, Mandal D, Byrne M, et al. Guidelines for the management of vulvodynia. Br J Dermatol 2010;162:1180–1185.
30. Reed BD, Caron AM, Gorenflo DW, Haefner HK. Treatment of vulvodynia with tricyclic antidepressants: Efficacy and associated factors. J Low Genit Tract Dis 2006; 10:245–251.
31. Tribo MJ, Andion O, Ros S, et al. Clinical characteristics and psychopathological profile of patients with vulvodynia: An observational and descriptive study. Dermatology 2008; 216:24–30.

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2. Johanna Ekdahl, Linnea Engman, Steven J Linton. 2017. Vulvovaginal pain from a fear-avoidance perspective: a prospective study among female university students in Sweden. *International Journal of Sexual Health* **6**, 00-00. [Crossref]
3. Ahinoam Lev-Sagie, Asia Kopitman, Amnon Brzezinski. 2017. Low-Level Laser Therapy for the Treatment of Provoked Vestibulodynia—A Randomized, Placebo-Controlled Pilot Trial. *The Journal of Sexual Medicine* **14**:11, 1403-1411. [Crossref]
4. Reed Barbara D.. 2017. Candida Vulvovaginitis and Vulvodynia: The Mystery Continues. *Journal of Women's Health* **26**:10, 1045-1046. [Citation] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
5. Barbara D. Reed, Melissa A. Plegue, Siobán D. Harlow, Hope K. Haefner, Ananda Sen. 2017. Does Degree of Vulvar Sensitivity Predict Vulvodynia Characteristics and Prognosis?. *The Journal of Pain* **18**:2, 113-123. [Crossref]
6. Barbara D. Reed, Ananda Sen, Sioban D. Harlow, Hope K. Haefner, Richard H. Gracely. 2017. Multimodal Vulvar and Peripheral Sensitivity Among Women With Vulvodynia. *Journal of Lower Genital Tract Disease* **21**:1, 78-84. [Crossref]
7. Maria L. Boccia. 2016. How Do Early Life Experiences Modulate Sexual Function, Stress, and Pain? The Role of Serotonin in Sexual Function. *Current Sexual Health Reports* **8**:3, 198-205. [Crossref]