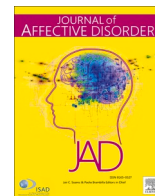




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Assessment of anxiety, depression and somatization in women with vulvodynia: A systematic review and META-analysis

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ABSTRACT

Objective: To assess the presence of anxiety, depression and somatization in women with vulvodynia.

Methods: The search for articles was performed in the electronic databases MEDLINE, via PubMed, EMBASE, LILACS and the American Psychological Association (PsycINFO). A search strategy was developed using the following terms: “Vulvodynia” and “psychological symptom” and their respective synonyms. The search was limited to human studies and no language restriction.

Results: After the screening process, 10 studies met the eligibility criteria and were included in this review. The studies were published between 1993 and 2017, with 2886 participants, of which 912 are cases and 1974 are controls. Meta-analysis of included studies revealed a significant difference between groups in depression outcomes (DMP: 0.75; 95 % CI: 0.41 to 1.10; $p < 0.0001$; I2: 28 %), anxiety (DMP: 1.22; 95 % CI: 0.84 to 1.59; $p < 0.00001$; I2:0%) and somatization (DMP: 1.31; 95%CI: 0.80 to 1.82; $p < 0.00001$; I2: 46 %).

Conclusion: Through the meta-analyses, significant associations were observed between vulvodynia and depression, anxiety and somatization.

1. Introduction

According to the International Society for the Study of Vulvovaginal Disease (ISSVD), vulvodynia is defined as a chronic discomfort or pain in the vulva lasting at least three months (Moyal-Barracco, 2003). Women with this condition experience severe irritation, burning, itching, and even a “stinging” sensation in the vulvar region, and for diagnosis, these symptoms should not be associated with any other infection, neoplasm, or disease (Haefner, 2007).

It becomes complex to estimate the magnitude of vulvodynia. A population-based study in the United States, with 2542 women, estimated the prevalence at 8.3 % to 9.2 % (Reed et al., 2012a). Another 2003 population-based study of 4915 women estimated a prevalence of vulvodynia at 16 % (Harlow and Stewart, 2003). The difference in prevalence found between the studies may be due to the methodology of the studies, as one was conducted by telephone recruitment and completion of a self-administered survey, while the other used town census directories.

The etiology is still not well known and is usually multifactorial, with

some factors considered potential risks: infection and inflammation (Nguyen et al., 2009), genetic polymorphisms and the immune system (Gerber et al., 2003; Jeremias et al., 2000) neuroinflammation (Tympanidis et al., 2003; Tympanidis et al., 2004), comorbidities and chronic pain (Reed et al., 2012b), pelvic floor muscle dysfunction (Gentilcore-Saulnier et al., 2010) and psychosocial factors (Khander et al., 2011).

Vulvodynia can affect many different areas of a woman's life: quality of life, sexual relationships, daily well-being, and psychological. There is a correlation between psychological states such as depression, anxiety, stress, somatization, and others in the appearance and level of pain of these women affected by vulvodynia, and some hypotheses bring that these factors can trigger vulvodynia and other hypotheses bring that pain can be a triggering factor (Reed et al., 2012b; Monteiro, 2013; Monteiro et al., 2015).

According to the International Classification of Diseases (ICD-11), depression can be divided into single episode depressive disorder (6A70) and recurrent depressive disorder (6A71), which is characterized by depressed mood, in which there is sadness, irritability, and feeling of emptiness, or the loss of pleasure accompanied by cognitive,

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neurovegetative or behavioral symptoms that can affect the functional capacity of people (OMS, 2018). Anxiety as a disorder is characterized by excessive fear and worry persistently and makes the person not have much control over the feeling, causing symptoms such as tension, restlessness, irritability, and fatigue, in addition in cases of generalized anxiety disorder there may be shortness of breath, palpitations, nausea, tachycardia, muscle pain and increased pressure (Linton and Shaw, 2011; Ruscio et al., 2017). Somatization does not have a specific meaning, according to Fortes and collaborators (2002) it concerns the presentation of somatic complaints, on account of psychological causes, but are attributed by the patient to an organic cause (Fortes, 2002). Thorton states that it is suffering and conflict converted into somatic complaints in an unconscious attempt to reduce intrapsychic tension (Lobato, 2010).

To reduce the symptoms of pain in women committed by vulvodynia, it is important that a multidisciplinary treatment is performed, to encompass the most diverse aspects of vulvodynia. Among these treatments, one can highlight pharmacological, psychological, and physical therapies, such as physiotherapy for the pelvic floor. The evaluation of levels of depression, anxiety, stress, and other psychosocial issues provides a better psychological approach to the treatment of these women (De Andres et al., 2016; Goldstein et al., 2016).

Thus, this research aimed to evaluate the presence of anxiety, depression and somatization in women with vulvodynia through a systematic review and meta-analysis.

2. Methods

Was performed a systematic review according to a prospective protocol using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (Page et al., 2021). This study was registered with PROSPERO (Prospective International Register of Systemic Reviews, <http://www.crd.york.ac.uk/prospero>) under protocol number CRD42022337208.

2.1. Eligibility criteria

Were included observational studies that evaluated women with vulvodynia and their association with psychosocial factors, in women over 18 years old compared to controls without vulvodynia who underwent psychosocial analyses, performed through multiple-choice scales or self-report questionnaire, were included. Exclusion criteria were studies without controls, that presented another vulvar condition as a control, and those that did not evaluate psychosocial outcomes. The research question was formulated through the PECOT strategy (P: population; E: exposure; C: comparison; O: outcomes; T: type of study).

Population: Women over 18 years of age;

Exposure: Vulvodynia;

Comparison: Controls without vulvodynia;

Outcomes: Psychosocial factors (such as depression, anxiety, somatization);

Type of Study: Observational studies (case-control; cross-sectional).

2.2. Search strategy

The search was conducted in the electronic databases: MEDLINE, via PubMed, EMBASE, LILACS, and American Psychological Association (PsycINFO), using the following terms: “Vulvodynia”, “psychological symptom” and their respective synonyms, queried in Medical Subject Headings (MeSH). A search was performed using a sensitive filter by combining the different synonyms with the Boolean operators “OR” and “AND”. The search was limited to human studies, with no language restriction. In addition, the reference lists of all selected primary studies were checked for possible additional relevant citations.

2.3. Study selection

Two reviewers (S.D-F and A.C.R.C.) independently evaluated the titles and abstracts of all articles identified by the searches. The screening process was conducted via the Rayyan website (rayyan.qcri.org). Once the authors excluded studies that did not meet the criteria, the remaining studies were read in full, also by two reviewers (S.D-F and A.C.R.C.), selecting those that met the inclusion criteria for this systematic review. A third review author (M.I.R.) resolved any discrepancies in the selection of the included studies.

2.4. Data extraction

The articles selected for inclusion had their data extracted by filling out a collection form composed of author, year, country, objectives of the study, characteristics of the patients, methods, instruments used, information on psychosocial outcomes, results, and conclusion of each study included.

The procedure was carried out by two reviewers (S.D-F. and A.C.R.C.) independently, and a third reviewer (M.I.R.) was consulted when necessary.

2.5. Quality assessment and risk of bias

To assess the risk of bias, two reviewers (S.D.F and A.C.R.C.) independently evaluated each selected study using the Newcastle-Ottawa Quality Index Scale. This tool is presented through a “star system,” which evaluates observational case-control type studies based on eight items and cross-sectional studies based on seven items, categorized into the following three groups: (1) selection of study participants, (2) population comparability, and (3) checking whether the exposure or outcome includes any risk of bias, selection bias, or loss-to-follow-up bias.

The higher the number of stars, the better the quality of the study. Case-control studies with a score between seven and nine stars were considered to be of high quality and low risk, scores of four to six stars represent moderate quality and risk, and studies with zero to three stars indicate low quality and high risk of bias. In cross-sectional studies nine to ten stars were considered very good studies, seven to eight points were considered good studies, five to six points were considered satisfactory studies, and zero to four points were considered unsatisfactory studies. Studies with scores greater than seven have a low risk of bias, studies with scores between five and six have an unclear/intermediate risk of bias, and studies with scores between zero and four have a high risk of bias (Modesti et al., 2016).

2.6. Data analysis

The results obtained were expressed through tables and graphs. Forest plot were made to evaluate the outcomes of depression, anxiety, and somatization in women with vulvodynia and controls without vulvodynia. The studies had continuous outcomes, so standardized mean difference (SMD) with 95 % confidence intervals (95 % CI) was used using RevMan 5.4 software (The Nordic Cochrane Center, Copenhagen, Denmark).

Study heterogeneity was determined using the I^2 statistic, in which 0 % to 30 %: may not be important; 40 % to 60 %: may represent moderate heterogeneity; 50 % to 90 %: may represent substantial heterogeneity; and 75 % to 100 %: considerable heterogeneity. When heterogeneity was present, a random effect model was used to calculate the estimates. When heterogeneity was absent, a Mantel-Haenszel fixed effect model was used (Deeks et al., 2019).

3. Results

The initial search results from the database search strategy identified

473 studies were found, of which 103 were duplicates and were therefore excluded from the study, leaving 370 studies for screening of titles and abstracts. Of these, 348 were excluded for not qualifying for full-text reading. Of these, 12 studies were excluded for not meeting the inclusion criteria, 6 for evaluating another population, 4 for having a different control group, 1 study was unable to obtain the full article, and 1 for being in another language. Resulting in 10 studies included in this review (Khander et al., 2011; Arnold et al., 2006; Arnold et al., 2007; Bodden-Heidrich et al., 1999; Iglesias-Rios et al., 2015; Jadresic et al., 1993; Reed et al., 2000; Stewart et al., 1994; Tribo et al., 2008; Wylie et al., 2004). The study selection process is summarized in Fig. 1.

3.1. Characteristics of the included studies

Studies published between the years 1993 and 2017, conducted in the following countries were included: the United States of America (5), Germany (1), Canada (1), the United Kingdom (2), and Spain (1). In total, the ten studies that were included in this review had 2886 participants, of which 912 women had vulvodynia (exposed group) and 1974 women did not have vulvodynia (control group). The age of the

participants ranged from 18 to 80 years. The characteristics of the included studies are presented in Table 1.

3.2. Analysis of the main outcomes assessed

The included studies evaluated different psychosocial outcomes of women with vulvodynia, and the main outcomes evaluated in the studies were: depression, which was evaluated by 10 studies, five studies evaluated anxiety, and five studies studied somatization. To evaluate these outcomes different scales were used, including self-report questionnaires and validated scales.

Data regarding the scales used to evaluate the outcomes of depression, anxiety, and somatization, as well as data regarding the results obtained by the included articles, were described in Table 2.

3.2.1. Assessment of depression

Among the included studies, all of them evaluated depression in women with vulvodynia, however, due to the methodological difference between the studies, it was possible to perform the meta-analysis with the studies of Bodden-Heidrich et al. (1999), Stewart et al. (1994) and

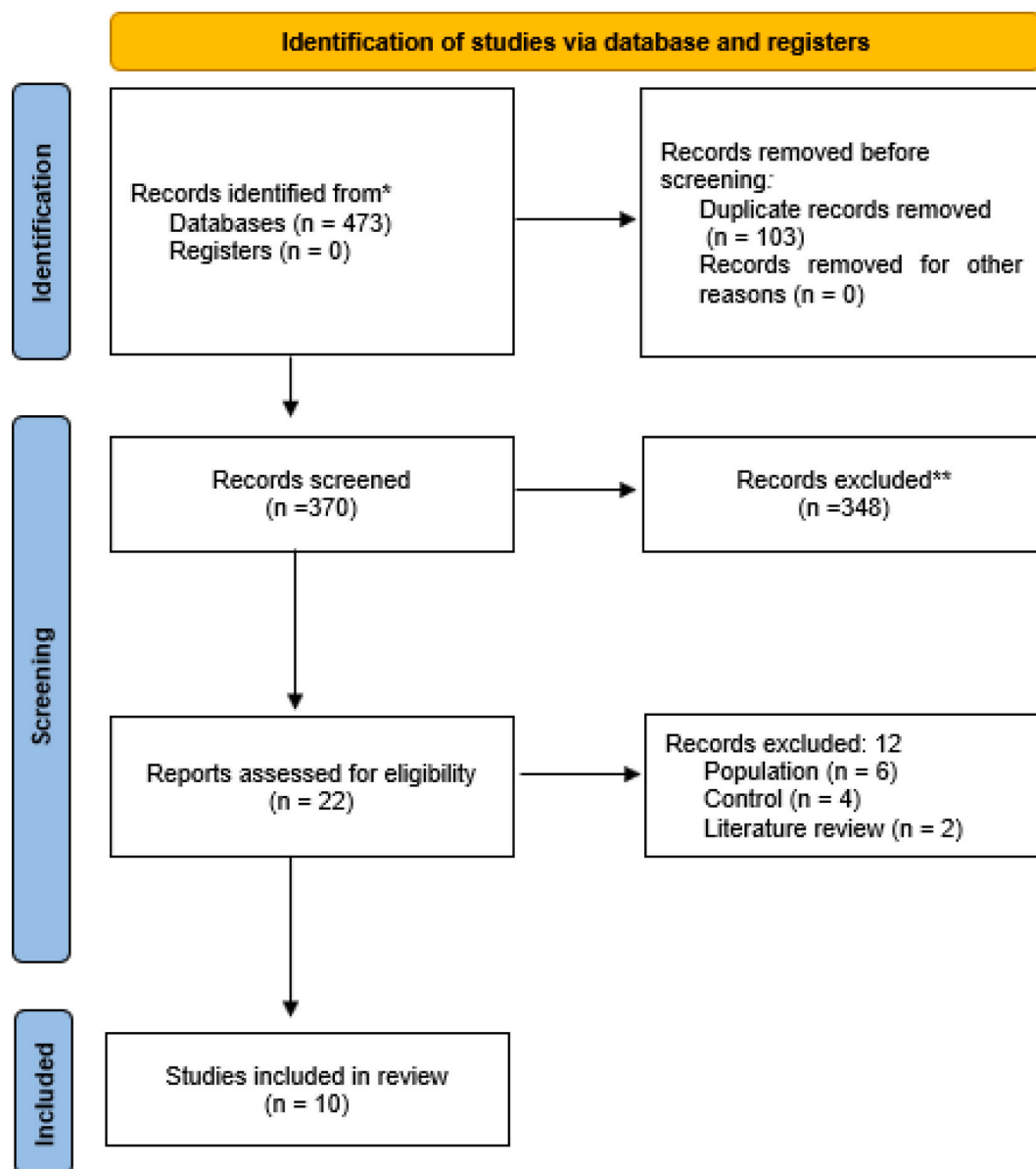


Fig. 1. Flowchart of the selection process of the included studies.

Table 1
Characteristics of the included studies.

Author/ year	Country	Type of Study	Objective	N Case	Age Case	N Control	Age Control	Conclusion
Arnold et al., 2006	USA	Case-Control	Compare the health history and health care utilization of women with vulvodynia to a control group reporting no gynecological pain.	77	43.1 (±13.7)	208	51.1 (±10.5)	It showed that vulvodynia substantially affects the quality of life and sexual health. Reduced quality of life is significantly associated with vulvodynia
Arnold et al., 2007	USA	Case-Control	To assess the prevalence of vulvodynia symptoms in a sample of US women and compare health characteristics of symptomatic and asymptomatic women	100	18–80	325	18–80	North American English-speaking women confirm significant disruption to personal life, including sexual function and overall quality of life, attributable to chronic vulvar pain.
Bodden-Heidrich et al., 1999	Germany	Case-Control	To evaluate the psychological aspects of patients with vulvodynia in comparison to patients with chronic pelvic pain	36	38	34	Not Informed	There were significant differences between the vulvodynia group and the control group concerning depression.
Iglesias-Rios et al., 2015	USA	Cross-Sectional	To describe the magnitude of the association of depression and PTSD with the presence of vulvodynia	221	45.0 (±12.37)	965	46.0 (±12.8)	This article documented a moderate association between depression and the risk of having vulvodynia
Jadresic et al., 1993	United Kingdom	Cross-Sectional	To estimate the prevalence of psychiatric morbidity in the patients seen at the clinic and to test the hypothesis that women with vulvodynia would have a higher level of psychological distress than other clinicians.	10	52.5 (±17.7)	41	54.5 (±21.4)	There is little evidence that women with vulvodynia have higher rates of psychiatric morbidity than those with other vulvar diagnoses. The psychiatric prevalence rate in women attending a clinic for vulvar problems is high, although comparable to that reported in studies of hospital outpatient populations.
Khander et al., 2011	USA	Case-Control	Determine whether antecedent-diagnosed depression and anxiety are associated with the risk of vulvodynia and whether vulvodynia increases the risk of the new or recurrent onset of depression or anxiety.	240	30–50	240	30–50	DSM-IV diagnosed mood and anxiety may influence the development of unexplained vulvar pain. Furthermore, this study establishes that the development of vulvodynia can lead to new or recurrent mood or anxiety disorders.
Reed et al., 2000	USA	Cross-Sectional	To determine whether the psychological, somatization, sexual pain and functionality functions of women with vulvodynia differ from women with chronic pelvic pain and women without vulvodynia	31	42,8	23	42,4	The evidence supports that women with vulvodynia and chronic pelvic pain have more psychological disorders.
Stewart et al., 1994	Canada	Case-Control	To assess whether women with vulvodynia differ psychologically from women with other gynecological conditions or from women without vulvodynia.	32	43 (±14,6)	31	43 (±14,6)	In general women with vulvodynia are significantly more anxious and have more somatization. In addition to a worse general health condition.
Tribo et al., 2008	Spain	Case-Control	This study aims to evaluate the medical and psychopathological profile of patients affected by vulvodynia seen at the dermatology outpatient clinic.	80	46.9 (±13.0)	20	41.2 (±10.9)	Patients with vulvodynia are affected by various psychological disorders. From a therapeutic point of view, the use of antidepressants, which act on serotonin and noradrenergic drugs, can be a useful option in the frequent, disturbing and disappointing disease.
Wylie et al., 2004	United Kingdom	Cross-Sectional	Compared the prevalence of psychological dimensions across three subgroups of dermatology patients. The groups were composed of women with vulvovestibulitis, women with vulvodynia, and women attending the dermatology clinic for another disease, not vulvar skin condition	85	41.5 (±13,95)	87	43.5 (±13,32)	These findings warrant further study and perhaps replication with a non-patient group. It is also important that we begin to ascertain more qualitative information from this patient group about their perceptions of their experience of living with these vulvodynia symptoms.

Legend: USA = United States of America; PTSD = Posttraumatic Stress Disorder.

Tribo et al. (2008). The main methodological difference between the studies, which made it impossible to make the comparison, concerns the different scales used to assess depression. The assessment of the depression outcome was performed by comparing three case-control studies, totaling 148 women with vulvodynia and 85 controls without vulvodynia.

Through meta-analysis, it was possible to find a significant difference between the groups evaluated for depression, presenting a Standardized Mean Difference (SMD) of -0.75 , with a 95 % Confidence Interval (CI) of -1.10 to -0.41 ($p < 0.0001$; I² of 28 %; 233 participants), the random effect was used in the meta-analysis due to the heterogeneity presented (Fig. 2). From the analysis of the results obtained, it was possible to observe that women with vulvodynia presented higher depression scores

when compared to women without vulvodynia.

3.2.2. Assessment of anxiety

Of the studies included in this review, five evaluated the outcome of anxiety in women with vulvodynia, because of the methodological differences between the studies that evaluated the outcome, it was possible to perform the meta-analysis with the studies of Stewart et al. (1994) and Tribo et al. (2008). The evaluation of the anxiety outcome was performed by comparing two case-control studies, totaling 112 women with vulvodynia and 51 controls.

Through meta-analysis, it was possible to find a significant difference between the groups evaluated for anxiety, presenting an SMD of -1.22 , with 95 % CI of -1.59 to -0.84 ($p < 0.00001$; I² of 0 %; 163

Table 2
Results of the Depression, Anxiety and Somatization outcomes.

Author/year	Scales used	Depression		Anxiety		Somatization		Main Results
		Case	Control	Case	Control	Case	Control	
Arnold et al., 2006	Depression: Self-reported	22/77 29.3 %	46/208 22.8 %	–	–	–	–	Although cases and controls reported similar levels of stress, cases were more likely ($p < 0.001$) to report a worse overall quality of life. Vulvodynia was significantly associated with worse quality of life. There were no significant differences in ratings of self-reported stress or history of depression.
Arnold et al., 2007	Depression: Self-reported	46/100 46 %	72/325 22 %	–	–	–	–	
Bodden-Heidrich et al., 1999	Depression and Somatization: Freiburg personality inventory and Gieben Test	Mean +/- SD: 5.60 +/- 1.91	Mean +/- SD: 4.26 +/- 1.25	–	–	Mean +/- SD: 6.60 +/- 1.65	Mean +/- SD: 4.15 +/- 1.41	Quality of life and personal stress levels were higher in the cases, although the differences were not significant
Khander et al., 2011	Anxiety and Depression: SCID	35 (14.6 %)	26 (10.8 %)	10 (4.2 %)	6 (2.5 %)	–	–	There were significant differences in the vulvodynia group and the control group concerning depression, a tendency to somatization, and emotional instability. Women with vulvodynia were 1.7 times more likely to have a new or recurrent mood disorder or anxiety compared to women with no history of vulvar pain.
Stewart et al., 1994	Brief Symptom Inventory Somatization: SOM; Depression: DEP e CES-D; Anxiety: Anxiety Subscale;	DEP-0.69 (±0.69) CES-D-1.95 (±0.27);	DEP-0.17 (±0.24) CES-D-1.7 (±0.20);	0.97 (±0.70)	0.38 (±0.37)	0.80 (±0.70);	0.22 (±0.31);	All women with vulvodynia were compared with patients with vulvar pathology without vulvodynia. Women with vulvodynia scored significantly higher on general health questions.
Tribo et al., 2008	Anxiety: HADS e HRSA; Depression: HADS	4.58 (± 4.32)	2.80 (± 2.78)	HADS: 7.91 (± 4.93)	HADS: 5.25 (± 3.45)	HRSA: 19.46 ± 10.21	HRSA: 5.89 ± 6.56	The main diagnoses were generalized anxiety ($n = 15$), depression-anxiety syndrome ($n = 6$), and somatizing disorder ($n = 6.7$). Other diagnoses were depression ($n = 2$), personality disorder ($n = 2$) anxiety ($n = 2$), psychosis ($n = 2$), bulimia ($n = 1$), epilepsy ($n = 1$), insomnia ($n = 1$), and bipolar disorder ($n = 1$). The control group differed significantly in the mean for all disorders measured.
Wylie et al., 2004	Anxiety, Depression, Somatization: SCL-90R	63.08 (± 8.68);	55.39 (± 11.13)	57.92 (± 11.94)	51.62 (±11.75);	58.61 (±11.37);	53.99 (±10.87);	A significant difference with higher levels of somatization ($p = 0.033$), obsessive-compulsive ($p = 0.002$), interpersonal sensitivity ($p = 0.017$), depression ($p = 0.001$), anxiety ($p = 0.025$), hostility ($p = 0.006$), phobic ($p = 0.009$), paranoia ($p = 0.005$) and psychoticism ($p = 0.001$) when compared to the dermatological population. Women with vulvodynia were more likely to screen positive for depression (20.8 %) than women with short-term or past vulvar symptoms (12.5 %) and women without vulvodynia (13.1 %). Women with vulvodynia were more likely to screen positive for PTSD (20.0 %) than women without vulvodynia (9.5 %).
Iglesias-Rios et al., 2015	Depression: Health Questionnaire depression scale	46 (20.8 %);	126 (13.1 %)	–	–	–	–	The mean total GHQ-28 score for the vulvodynia group (14.1) was lower than that for the non-Vulvodynia group (20.3). This difference was not statistically significant at the 0.025 level when compared to an independent samples t -test
Jadresic et al., 1993	Anxiety, Depression, Somatic symptoms: GHQ	0.2 (0.4);	1.7 (3.0);	3.2 (3.2);	5.6 (4.3)	3.7 (3.0)	5.7 (4.1)	Women with vulvodynia did not have significantly more reports of somatic problems compared to the control group
Reed et al., 2000	Depression: BDI; Somatic complaints: Modified Somatic Perception Questionnaire	7.9	5.9	–	–	29.3	26.2	

Legend: BDI = Beck Depression Inventory; CESD = Center for Epidemiologic Studies Depression Scale; DEP = Depression Subscale; DP = Desvio padrão; GHQ = The General Health Questionnaire; HADS = Hospital Anxiety and Depression Scale; HRSA = Hamilton Rating Scale for Anxiety; SCID = Structured Clinical Interview for DSM; SCL Symptom Checklist- 90-R; SOM = Somatization Subscale;

participants), the fixed effect was used in the meta-analysis (Fig. 3). From the analysis of the results obtained, it is observed that women with vulvodynia have a higher anxiety score when they were compared with women without vulvodynia.

3.2.3. Somatization assessment

Among the included studies, five evaluated somatization in women with vulvodynia, however, due to the methodological difference

between the studies it was possible to perform the meta-analysis with the studies of Bodden-Heidrich et al. (1999) and Stewart et al. (1994). The evaluation of the somatization outcome was performed by comparing two case-control studies, totaling 68 women with vulvodynia and 65 controls.

Through meta-analysis, it was possible to find a significant difference between the groups evaluated for somatization, presenting an SMD of -1.31, with 95 % CI of -1.82 to -0.80 ($p < 0.00001$; I2 of 46 %; 133

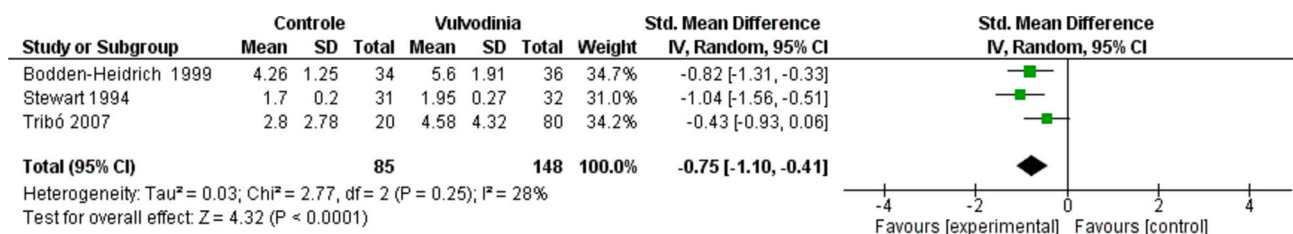


Fig. 2. Meta-analysis of the comparison of depression between women with vulvodinia and controls.

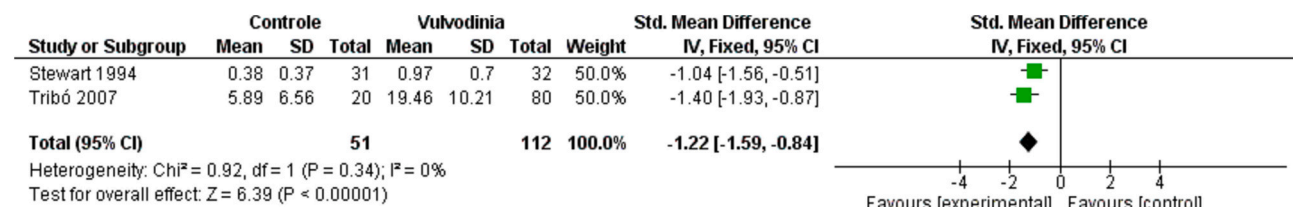


Fig. 3. Meta-analysis of the comparison of anxiety between women with vulvodinia and controls.

participants), the random effect was used in the meta-analysis, due to the heterogeneity presented (Fig. 4). It was observed from the analysis of the results that women with vulvodinia have higher somatization scores when compared to women without vulvodinia.

3.3. Analysis of the secondary outcomes evaluated

In addition to the assessment of depression, anxiety, and somatization, some studies also assessed the following aspects: stress (3 studies), quality of life (2 studies), Obsessive Compulsive Disorder (OCD) (2 studies), Paranoia (2 studies) and Psychosis/Psychoticism (2 studies).

In addition to these endpoints, Posttraumatic Stress Disorder (PTSD) (1 study), Emotional instability (1 study), Social dysfunction (1 study), Phobia/Phobic anxiety (1 study), Interpersonal sensitivity (1 study), Hostility (1 study) were also assessed. The secondary endpoints, mentioned above, were described in Table 3.

3.4. Quality assessment and risk of bias

To assess the risk of bias, the Newcastle-Ottawa Quality Assessment Scale adapted for each type of design was used. Six articles were analyzed using the scale adapted for case-control studies and four articles were analyzed using the scale adapted for cross-sectional studies. Concerning the case-control studies, biases were found in the selection and exposure processes.

The study by Bodden-Heidrich et al. (1999) showed low quality and high risk of bias because there was no description of the selection process, low representativeness of cases, controls obtained from the clinic, no assessment of additional factors, no information on blinding, and no respondents. The study by Khander et al. (2011) showed moderate quality and moderate risk of bias as there were no examinations for selection, does not assess additional factors, and does not provide blinding information. Stewart et al. (1994) presented moderate quality

and moderate risk of bias given that they obtained controls from one department and does not describe blinding and non-respondents. Arnold et al. (2007) showed high quality and low risk of bias, although they did not evaluate cases and used self-reported scaling. Tribo et al. (2008) presented a high quality and low risk of bias, despite the low representativeness of the cases and does not talk about blinding. The study by Arnold et al. (2006) presented a high quality and low risk of bias, despite using self-reported scales.

The cross-sectional studies presented selection biases, given that information about the participant selection process is missing. The studies by Jadresic et al. (1993) and Reed et al. (2000) presented four points, being considered unsatisfactory studies with a high risk of bias. Iglesias-Rios et al. (2015) presented six points, being considered satisfactory studies and unclear/intermediate risk of bias. Wylie et al. (2004) presented five points, being considered satisfactory studies and unclear/intermediate risk of bias. The results of the Newcastle-Ottawa Quality Assessment Scale are shown in Table 4.

4. Discussion

This systematic review evaluated the evidence about psychosocial changes in women with vulvodinia. Our study showed that women with vulvodinia had higher scores on the outcomes of anxiety, depression, and somatization when compared to women without vulvodinia.

Several authors have conducted studies evaluating women with vulvodinia in various aspects of life, and in the literature, some results corroborate the findings of this review. Study conducted by Tribó et al. (2020), used a descriptive observational method to analyze the pain of women with vulvodinia and correlate it with symptoms of anxiety and depression. 110 patients with vulvodinia and with a mean age of 43.4 years were studied. The Hamilton Anxiety Scale (HAM-A) was used to assess anxiety and the Hospital Anxiety and Depression Scale (HADS) assessed both anxiety and depression. These symptoms were observed in

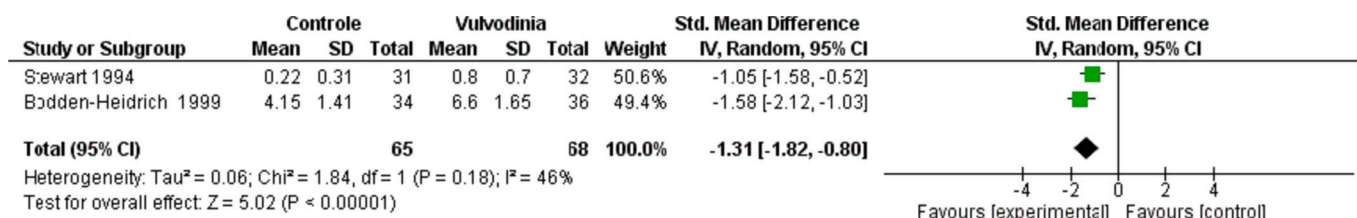


Fig. 4. Meta-analysis of the comparison of somatization between women with vulvodinia and controls.

Table 3
Results of the secondary outcomes evaluated by the studies.

Author/ year	Scales used	Outcomes	
		Case	Control
Arnold et al., 2006	Stress: Self-reported (0 to 10);	Stress: 5.9 (± 2.3);	Stress: 5.7 (± 2.4);
	Quality of life: Modified Ladder of Life scale.	Quality of life: 7.0 (± 1.9)	Quality of life: 8.2 (± 1.4)
Arnold et al., 2007	Stress: Self-reported (0 to 10);	Stress: 6.88;	Stress: 5.66;
	Quality of life: Self-reported (0 to 10);	Quality of life: 8.4	Quality of life: 8.9
Bodden-Heidrich et al., 1999	Emotional instability: Freiburg personality inventory and Gieben Test	Emotional instability: 5.39 +/- 1.65	Emotional instability: 4.79 +/- 1.2
	Iglesias-Rios et al., 2015	PTSD: Primary care PTSD screen	PTST: Yes- 44 (19.9 %) Suggestive - 25 (11.3 %)
Jadresic et al., 1993		Social dysfunction: GHQ;	Social dysfunction: 7. (1.4)
	Stewart et al., 1994	<u>Brief Symptom Inventory</u>	OCD:0.79 (±0.58); Phobia: 0.32 (±0.44);
Wylie et al., 2004		OCD: OBS; Phobia: PANX Paranoia: PAR Psychosis: Psychotic Subscale;	Paranoia: 0.68 (±0.83); Psychosis: 0.48 (±0.63);
	Wylie et al., 2004	OCD, Anxiety phobia, Paranoia, Interpersonal sensitivity; Hostility; Psychoticism: SCL-90R	OCD: 61.10 (±11.37); Anxiety phobia: 54.61 (±12.40); Paranoia: 55.87 (± 11.42); Interpersonal sensitivity; 61.61 (±11.46); Hostility: 57.69 (±11.32); Psychoticism; 59.63 (±12.06)

Legend: GHQ = The General Health Questionnaire; OBS = Obsessive Compulsive Subscale; PANX = Phobic Anxiety Scale; PAR = Paranoid Subscale; SCL-90R = Symptom Checklist- 90-R; PTSD = Post traumatic Stress Disorder; OCD = Obsessive-compulsive disorder.

81 patients, and the mean HADS-A score was 9.0 ± 4.2 (borderline abnormal), and the mean HADS-D score was 5.2 ± 4.8 (normal). The mean HAM-A score was 12.3 ± 8.4, in which 74.1 %; (60 women) with mild anxiety (score ≤ 17), 17.3 % (14 women) with mild to moderate anxiety (score 18–24), 7.4 % (6 women) with moderate to severe anxiety (score 25–30), and 1.2 % (1 woman) with severe anxiety. Thus, most patients had severe pain related to psychiatric comorbidities and decreased quality of life (Tribó et al., 2020).

Another study performed by Gates and Galask (2001), psychological and sexual functioning in women with vestibulitis were evaluated. Were included 52 women with vestibulitis and 46 controls without vestibulitis participated in the study, and the mean age of vestibulitis was 29.5 ± 6.65 years, while the mean age of controls was 34.7 ± 7.19. Women with vestibulitis had significantly higher depression scores (17.20 ± 11.87) than controls (7.82 ± 6.44). Except for the somatization subscale, women with vestibulitis reported significantly higher scores than controls on each subscale (Gates and Galask, 2001).

A subtype of vulvodynia also reported in the literature is provoked vestibulodynia (PVD), in which the pain in the vulvar vestibule region is triggered by vaginal penetration (insertion of an internal absorbent pad, gynecological exams, and sexual activity). The woman suffering from

Table 4
Quality assessment of the included studies using the Newcastle-Ottawa scale.

Author/Year	Selection				Comparability	Exposure/ Outcome			Total
	1	2	3	4		1	2	3	
Case-Control									
Arnold et al., 2006	*	*	*	*	**	-	*	*	8
Arnold et al., 2007	-	*	*	*	**	-	*	*	7
Bodden-Heidrich et al., 1999	-	-	-	*	*	-	*	-	3
Khandker et al., 2011	-	*	*	*	*	-	*	*	6
Stewart et al., 1994	*	*	-	*	**	-	*	-	6
Tribó et al., 2008	*	-	*	*	**	-	*	*	7
Cross-sectional									
Iglesias-Rios et al., 2015	*	-	-	**	*	*	*		6
Jadresic et al., 1993	*	-	-	-	*	*	*		4
Reed et al., 2000	*	-	-	-	**	*	*		4
Wylie et al., 2004	*	-	-	-	**	*	*		5

Legend: Quality assessment of included studies was performed using the Newcastle-Ottawa scale (NOS). Scales were used to assess case-control studies (six studies) and cross-sectional studies (four studies). For the case-control study, Bodden-Heidrich et al., 1999 scored 3/9 (low quality and high risk of bias), Khandker et al., 2011 and Stewart et al., 1994 scored 6/9 (moderate quality and moderate risk of bias), remaining studies scored above seven stars, considered high-quality studies and low risk of bias. For the cross-sectional studies, Iglesias-Rios et al., 2015 scored 6/9 (satisfactory studies and unclear/intermediate risk of bias), Wylie et al., 2004 scored 5/10 (satisfactory studies and unclear/intermediate risk of bias), Jadresic et al., 1993 and Reed et al., 2000 scored 4/9 (unsatisfactory studies and high risk of bias).

Case-Control Studies: Selection: 1) Is the case definition adequate? 2) Representativeness of cases; 3) Selection of controls; 4) Definition of controls; Comparability: 1) Comparability of cases and controls based on design or analysis; Exposure: 1) Verification of exposure; 2) The same method of verification for cases and controls; 3) Non-response rate.

Cross-sectional study: Selection: 1) Sample representativeness; 2) Sample size; 3) Non-responders; 4) Exposure verification (risk factor); Comparability: 1) Subjects in different outcome groups are comparable, based on study design; Outcome: 1) Outcome assessment; 2) Statistical test;

provoked vestibulodynia ends up feeling a burning in the vulvar region, which may entail itching, a sensation of pressure on the site, and sharp pain (Henzell et al., 2017). Dargie et al. (2017) sought to determine whether women with PVD had psychosocial difficulties when compared to controls and participants with post-herpetic neuralgia. Thirty women with neuralgia were included, 65 with PVD and 108 controls, and aspects of depression, stress, and anxiety were assessed. It was observed that women with PVD, obtained a score of depression of 14.72 ± 11.65 and 11.84 ± 10.09 for controls. For anxiety, the PVD obtained 40.42 ± 12.97, while controls obtained 36.52 ± 10.97. Regarding stress, the women without PVD, presented 14.36 ± 7.24, while women with PVD presented 16.89 ± 8.86. Thus, they observed that the pain of women with PVD was restricted to certain activities, and they tended to present symptoms of depression, stress, anxiety, and sleep disorders, similar to those with other pain conditions. Furthermore, women with PVD report a great deal of pain catastrophizing and pain anxiety, highlighting the cognitive processes that may be at play (Dargie et al., 2017).

Concerning somatization, this study found higher scores for women with vulvodynia when compared to women without vulvodynia. The study by Sutton et al. (2009), investigated psychosocial functioning, pain sensitivity, and associations between these variables in 50 women (25 with PVD and 25 without the condition), using The Physical Component Summary of the Short-Form-36 Health Survey (PCS-SF-36) questionnaire. Somatization was assessed, specifically functional impairment related to the physical symptom. The groups showed significant differences in the frequency of physical somatization complaints, women with PVD reported more (7.36 ± 4.26) than controls

(5.00 ± 3.34) ($p < 0.05$). A significant difference was also observed in functional somatization ($p < 0.05$), as women with PVD had significantly lower scores (77.10 ± 16.44) than the control (85.85 ± 9.56). Indicating that women with PVD report increased levels of somatization compared to controls (Sutton et al., 2009).

In addition to the included studies assessing the aspects related to depression, anxiety, and somatization, two studies also researched the quality of life of this population, and it was observed that women with vulvodynia presented a worse overall quality of life. Ponte et al. (2009) conducted a cross-sectional study to understand the impact of vulvodynia on the quality of life of affected women. The sample consisted of 101 patients with vulvodynia with a mean age of 42 ± 16 and 179 patients with other vulvar conditions with a mean age of 45 ± 17, and dermatology-related quality of life was measured with Skindex-29. They observed that in the symptom's domain, patients with vulvodynia had worse quality of life (50 ± 17) than patients with many dermatological disorders, such as psoriasis, (42 ± 21) and without skin disease (14 ± 12). In the emotions and functioning domains, women with vulvodynia had significantly worse quality of life (50 ± 20 emotions and 44 ± 22 functioning) than patients with dermatological disorders, such as psoriasis, (39 ± 27 emotions and 23 ± 27 functioning) and without skin disease (9 ± 13 emotions and 4 ± 8 functioning). Women with vulvodynia were significantly more likely than patients with other vulvar conditions to report a history of depression (47 % vs 28 %, $P = 0.002$) (Ponte et al., 2009).

Regarding the pain experienced by women and its relationship with psychological factors, Chisari and Chilcot (2017) evaluated a biopsychosocial approach in women with vulvodynia, examining factors associated with pain severity and interference, being included 335 women with 34.8 ± 9.6 years of age. The Hospital Anxiety and Depression Scale (HADS) was used to assess the psychological distress (depression and anxiety) of the participants, and they obtained a mean of 18.25 ± 8.04 on this scale, thus noting that all psychosocial variables were significantly correlated with pain. The authors concluded that there is greater psychological distress, significantly associated with increased pain severity and interference (Chisari and Chilcot, 2017).

It was observed in this review and in the general literature that there is a relationship between chronic pain in women with vulvodynia, as well as the psychosocial changes that are found in this population. Chronic pain is an important public health problem, given that it affects the adult population with high prevalence, and these patients who have chronic pain present symptoms commonly found in depression and anxiety, among them, changes in sleep, appetite, energy, libido, and irritability (Capela et al., 2009). The relationship between pain and mental disorders can be either cause, consequence, or bidirectional, this leads to the worsening of clinical symptoms and being more complex the clinical management of both conditions, being that people with chronic pain are twice as likely to present mental disorders (Kreling et al., 2006). Moreover, to understand in a physiological way the relationships between chronic pain and mental disorders are complex and there are some difficulties to unravel, because the pain process involves several mechanisms, such as interactions in neurotransmitters and receptors of the central nervous system, genetic influences, and inhibition of pain circuits (Pereira et al., 2017). Thus, it is suggested that preexisting characteristics may be activated at the onset of pain processes, and stress associated with chronic pain may trigger the onset of mental disorders in predisposed individuals (Pereira et al., 2017; Katz et al., 2015).

Women with vulvodynia present several complications since, besides the physical and psychological issues, negative consequences in interpersonal relationships and sexual activity are also found (Vasconcelos, 2020). It is known that quality of life is also related to sexual function, and is directly linked to well-being, thus, it is important to highlight that sexuality should be considered a dimension of health (Cunha, 2017). When sexual activity ceases to be pleasurable, it can lead to a greater number of negative thoughts and maladaptive cognitions leading to high stress, besides the fact that the dysfunction can directly affect emotions

making women feel ashamed and frustrated, and there may be abandoned and demands from partners, impacting the relationship (Ribeiro et al., 2013). One of the factors involved in this issue is body image, and women with higher body exposure anxiety had more pain during intercourse, lower sexual function, and lower sexual satisfaction (Chisari et al., 2021). Because of these impacts of vulvodynia on women's health, quality of life, and sexuality, a detailed and thorough assessment of the history of the vulvovaginal pain condition, medical history, and psychological status must be performed (Vasconcelos, 2020).

Because vulvodynia has a multifactorial origin, its treatment presents several difficulties, requiring multidisciplinary attention from psychologists, physicians, physical therapists, and other professionals (Monteiro et al., 2015). It is known that women with vulvodynia also have marital, social, professional, and/or family problems that can end up aggravating the condition. Psychological interventions are also effective in the treatment of vulvodynia, through an individual, couple, and also group therapies, and this intervention aims to improve women's quality of life, reduce pain, strengthen the couple's romantic relationship, and restore sexual function (Gómez-Sánchez et al., 2007). Although the main goal is pain reduction, it is recommended that the couple's therapy be maintained after reduction for the improvement of the couple's cognitions and behaviors (Vasconcelos, 2020). The individual needs of the women and the couple should be taken into account to be able to make the therapeutic planning, regarding the number of sessions, session time, and which modalities of therapy should be recommended (De Andres et al., 2016).

For the management of vulvodynia cognitive-behavioral therapy (CBT) is the most studied and the most used, this approach will condition the positive outcomes in pain management, improvement of sexual function, decreased catastrophizing of pain, and other negative thoughts (Vasconcelos, 2020). In the study by Masheb et al. (2009), they observed that CBT shows substantial improvement in pain, severity, disability, and affective distress when compared to supportive psychotherapy (Masheb et al., 2009). Thus, education in coping skills and pain self-management was useful in reducing psychological and sexual distress in women with pelvic pain, thus CBT appears to be an effective intervention for women with vulvodynia (De Andres et al., 2016). CBT often uses mindfulness, this technique is becoming more relevant in the treatment of vulvodynia, as it can help in the search for pain management and tolerance mechanisms, raise awareness of possible pain aggravation or relief and increase focus on positive life and relationship events (Brotto et al., 2015). With this, it is observed that psychological treatments for vulvodynia can be effective in achieving better outcomes and greater satisfaction, and it is important here to point out that although CBT is a widely studied approach, all approaches to psychology the potential in aiding pain reduction and increased resilience.

In summary, it is noteworthy that the results presented in this review, indicating that women with vulvodynia had higher scores on the outcomes of anxiety, depression, and somatization when compared to women without vulvodynia, align with established findings in psychosomatic medicine (Mascherpa et al., 2007). As limitations of this research, one can cite the number of studies available in the literature and consequently those that met the criteria of included articles, thus few studies could be evaluated in the meta-analysis, given the different methodologies and instruments used to assess psychosocial outcomes. In addition, most of the included studies had low methodological quality. There are still gaps in the research on this topic, and further investigations are needed within this area.

5. Conclusion

Our study demonstrated that there is a significant association between vulvodynia and the outcomes depression, anxiety and somatization. In conclusion, this systematic review sheds light on the profound psychosocial impact of vulvodynia, emphasizing the substantial burden it places on the lives of affected women. The consistent findings across

multiple studies, as presented here, confirm the association between vulvodynia and elevated levels of anxiety, depression, and somatization. These results resonate with the principles of psychosomatic medicine, demonstrating that physical symptoms and emotional well-being are intricately intertwined.

Furthermore, the association between vulvodynia and psychological distress highlights the bidirectional relationship between chronic pain and mental health. The coexistence of depression, anxiety, and somatization with chronic pain can exacerbate the severity of both conditions, making clinical management more complex. Therefore, a comprehensive assessment and individualized interventions are essential to address the specific needs of women living with vulvodynia. Furthermore, given the psychosocial complexity, we emphasize the relevance of a multidisciplinary approach to the treatment of vulvodynia that addresses not only physical pain but also psychological well-being and the quality of life of affected women.

In this regard, in contrast to the limited number of studies on the subject, we emphasize that evidence-based healthcare provides healthcare professionals with clear and up-to-date guidance on the most effective treatment options based on robust research and clinical outcomes. This ensures that women with vulvodynia receive interventions that have been rigorously evaluated for their safety and efficacy, thereby promoting more positive outcomes and a more informed and precise approach to managing this challenging condition.

Author statement

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