Bilaga 4 Tabeller över inkluderade studier/Table over included studies

SBU Utvärderar: Diagnostik och behandling av provocerad vulvodyni/Diagnostics and treatment of provoked vestibulodynia

Rapport nr: 326

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Table 1 Pharmacological treatment.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
Brown et al. 2018 [1] USA Bachmann et al. 2019 [2] USA	Study design: RCT, multicentre with crossover design Patient characteristics: Provoked localized vulvodynia. n=89. Mean age: 37 (SD 12).	Intervention: Oral gabapentin, 1200 – 3000 mg/day for 6-8 weeks (4 weeks titration +2 weeks maintenance +2 weeks dose-taper in each crossover phase) n=45. Control: Placebo tablets n=44. Follow-up time: 6 weeks post-allocation and 6 weeks after cross-over (data pooled). Drop-out: I: 12/45 (20%) C: 14/44 (32%).	Pain during intercourse: VAS (range 0-10), total crossover data, MD (95% CI): 0.0 (-0.9 to 0.8), n=27 (ns). Pain during tampon test: VAS (range 0-10), total crossover data, MD (95% CI): -0.3 (-0.7 to 0.1), n=83 (ns).	FSFI, total crossover data, adjusted MD (95% CI): 1.3 (0.4 to 2.2) n=63, p=0.008.	Serious adverse events: I: 0/45 (0%) C: 0/44 (0%) Mild adverse events, %: *Rhinitis:* I: 11.2 C: 4.5 *Dizziness:* I: 10.1 C: 3.4 *Nausea:* I: 8.9 C: 3.4 *Headache:* I: 7.9 C: 5.6 *Somnolence:* I: 7.9 C: 4.5 *Bacterial vaginosis:* I: 7.9 C: 4.5 *Fatigue:* I. 5.6 C: 1.1 (all ns).	Risk of bias Low Blinding: Patients and treatment providers blinded.

Author Year Reference Country	**Study design Patient characteristics**	**Intervention Control Follow-up time Drop-outs**	**Results:** **• Pain during intercourse** **• Pain at pressure**	**Results:** **• Sexual function/satisfaction** **• Quality of life** **• Anxiety** **• Depression**	**Results:** **• Adverse events**	**Risk of bias Blinding Comments**
Bornstein et al. 2010 [3] Israel	Study design: NRSI with prospective allocation, single-centre, 3-arm. Patient characteristics: Provoked localized vulvodynia. n=50. Mean age: 24.7 (SD 2.9)	Intervention: Nifedipine cream, 2% or 4%, topical self-administration 4 times daily for 6 weeks I-A (2%) n=10* I-B (4%) n=10*. Control: Placebo cream n=10*. Follow-up time: Immediately post-treatment and 3 months post-treatment. Drop-out: Total: 20/50 (not reported in relation to groups).	Pain during intercourse, VAS (range 0-100), mean (SD): *Post-treatment:* I-A: 61.9 (34.2) I-B: 72.5 (27.6) C: 48.1 (42.8) (ns). *3 months post-treatment:* I-A: 51.5 (36.1) I-B: 69.7 (36.6) C: 57.6 (40.4) (ns). Vulvar pain assessed with q-tip test (range 0-100), mean (SD): *Post-treatment:* I-A: 56.2 (35.5) I-B: 63.5 (34.2) C: 53.4 (35.4) (ns). *3 months post-treatment:* I-A: 47.0 (37.7) I-B: 73.5 (29.4) C: 52.7 (46.6) (ns).		Serious adverse events: I-A: 0/10 (0%) I-B: 0/10 (0%) C: 0/10 (0%). Mild adverse events: “mild irritation felt by some of the participants in the intervention groups”.	Risk of bias: Moderate Blinding: Patients, treatment providers and assessors blinded. Comments: *Number of participants after drop-outs.
Diomande et al. 2019	Study design: RCT, single centre, with a blinded phase	Intervention: I: Botulinum toxin A, 50 units (I-A) or 100 units (I-B)	Marinoff dyspareunia scale (range 0–3), median (IQR) I-A: 1.5 (0–2)		Serious adverse events: I-A: 0/12 (0%)	Risk of bias Low

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
[4] Switzerland	of 3 months and an unblinded exploratory phase (data not extracted). Patient characteristics: Provoked vestibulodynia, according to Friedrich criteria. n=33. Median age: 27 (IQR 24 to 30).	injected subcutaneously into the dorsal vulvar vestibulum at one occasion. n=12 (I-A) and 9 (I-B). Control: Placebo injection (saline) n=12. Follow-up time: 3 months post-allocation. Drop-out: I-A: 0/12 (0%) I-B: 1/9 (11%) C: 1/12 (8%).	I-B: 1.5 (0–3) C: 2 (1-2) (p=0.927). Vulvar pain assessed with cotton swab test, VAS (0-10), mean (SD): I-A: 6.2 (2.60) I-B: 6 (1.77) C: 6.5 (1.31). (p=0.857).		I-B:0/8 (0%) C: 0/11 (0%).	Blinding: Patients, treatment providers and assessors blinded.
Donders et al. 2012 [5] Belgium	Study design: RCT, single centre with crossover design (12+12 weeks separated by a 1-week washout period). Patient characteristics: Provoked localized vulvodynia. n=30.	Intervention: Cutaneous fibroblast lysate cream, topical self-administration of 0.2 mL twice daily for 12 weeks n=15. Control: Placebo cream n=15. Follow-up time: 4-, 12-, 17- and 25-weeks	Pain during sexual activity: VAS (range 0-10), patients with >1 point reduction: *4 weeks post-treatment (before cross-over):* I: 42% C: 15%. *12 weeks post-treatment (before cross-over):* I: 31% C: 0%. Total cross-over data*, VAS change from baseline,		Serious adverse events: I: 0/15 (0%) C: 0/15 (0%). Mild adverse events: I: 3/15 (33%) C: 1/15 (7%) (ns).	Risk of bias: Low Blinding: Patients, treatment providers and assessors blinded. Comment: *There was evidence for a second-order carryover

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
	Mean age: 27 (range 20 to 54)	post-allocation. Drop-out: I: 2/15 (13%) C: 2/15 (13%).	MD (95% CI): *4 weeks post-treatment:* 1.1 (-0.6 to 2.8), n=26, p=0.20. *12 weeks post-treatment:* 1.3 (0.1 to 2.5), n=26 p=0.037. Vulvar pain assessed with q-tip test, VAS (range 1-10), patients with >1 point reduction: *4 weeks post-treatment (before cross-over)*: I: 64% C: 69%. *12 weeks post-treatment (before cross-over):* I: 55%) C: 50%. Total cross-over data*, VAS change from baseline: *4 weeks post-treatment:* p=0.91. *12 weeks post-treatment:*			effect (p = 0.024).

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
			p=0.96.			
Farajun et al. 2012 [6] Israel	Study design: RCT, single centre. Patient characteristics: Provoked vestibulodynia. n=40. Mean age: Not reported (range 19 to 39).	Intervention: Enoxaparin, 40 mg self-administered injections subcutaneously in the abdominal region once daily for 90 days n=20. Control: Placebo injection (saline) n=20. Follow-up time: Immediately post-treatment and 3 months post-treatment. Drop-out: I:1/20 (5%) C: 1/20 (5%).	Pain during sexual intercourse, % reduction*: *3 months post-treatment:* I: 28.9 C: 4.4 (p=0.057). Vulvar pain assessed with q-tip test, % reduction in NRS (0-10): *Post-treatment:* I: 24.0 C: 13.1 (p=0.018). *3 months post-treatment:* I: 29.6% C: 11.2% (p=0.004).		Serious adverse events: "there were no significant side effects".	Risk of bias: Moderate Blinding: Patients, treatment providers and assessors blinded. Comment: *Data was derived from one of the following questionnaires used in the study: Brief Pain Inventory, short form McGill Pain Questionnaire or the International Society for the Study of Vulvovaginal Disease vulvodynia questionnaire
Foster et al. 2010 [7] USA	Study design: RCT, multicentre with four treatment arms.	Intervention: 3 treatment arms for 12 weeks: I-A: Topical lidocaine cream	Pain during intercourse: VAS (range 0-10) change from baseline, mean (SD): I-A: -1.92 (1.82) n=21	Index of sexual satisfaction (range 0-100), change from baseline, mean (SD):	Serious adverse events: I-A: 0/33 (0%) I-B: 0/33 (0%)	Risk of bias Low Blinding:

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
	Patient characteristics: Provoked localized vulvodynia. n=133. Mean age: 33 (inclusion criteria 18 to 50).	5%, administered 4 times/day + placebo tablets, n=33. I-B: Oral desipramine 150 mg/day + placebo cream, n= 33. I-C: Oral desipramine 150 mg/day + topical lidocaine cream 5% 4 times/day, n=34 Control: Placebo tablets + placebo cream, n=33. Follow-up time: Immediately post-treatment. Drop-out: I: 5/33 (15%) I-B: 6/33 (18%) I-C:8/34 (24%) C: 2/33 (6%).	I-B: -2.07 (2.31) n=21 I-C: -1.72 (1.99) n=21 C: -1.97 (2.47) n=26 (all comparisons ns). Pain during cotton swab test, VAS (range 0-3), change from baseline, mean (SD). I-A: -6.42 (7.90) n=32 I-B: -8.07 (10.23) n=32 I-C: -11.37 (8.00) n=34 C: -8.65 (6.59) n=33 (all comparisons ns).	I-A: 0.43 (11.71) n=24 I-B: -6.86 (10.30) n=28 I-C: -6.32 (10.43) n=30 C: 0.69 (9.28) n=28 (all comparisons ns). Becks Depression Inventory (range 0-63), change from baseline, mean (SD): I-A: -0.86 (5.90) n=30 I-B: -3.33 (5.26) n=27 I-C: -1.77 (7.58) n=32 C: -1.92 (5.44) n=29 (all comparisons ns).	I-C: 0/34 (0%) C: 0/33 (0%). Mild adverse events, %: I-A: 0/33 (0%) I-B: 1/33 (3%) I-C: 1/34 (3%) C: 0/0 (0%).	Patients and treatment providers blinded.
Haraldsson et al. 2020 [8] Sweden	Study design: RCT, single centre. Patient characteristics: Provoked	Intervention: Botulinum toxin A, 50 units injected bilaterally in the bulbocavernosus muscles, 2 treatments with 3 months interval.	Pain during sexual intercourse or tampon use, VAS (0-100), mean (SD): *Average during posttreatment period (from assessment at 3 and 6*	FSFI, mean (SD): *Average from assessment at 3 and 6 months:* I: 20.9 (6.8) C: 19.5 (5.9) MD: 1.37 (95% CI -0.90	Serious adverse events: I: 0/41 C: 0/42. Mild adverse events: ns (data not	Risk of bias: Low Blinding: Patients, treatment providers and

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
	vestibulodynia. n=88. Mean age: Not reported, (inclusion criteria 18 to 40).	n=44. Control: Placebo injection (saline) n=44. Follow-up time: 1.5-, 3-, 4.5- and 6-months post-allocation. Drop-out: I:3/44 (7%) C: 2/44 (5%).	*months):* I: 51.7 (25.7) C: 59.0 (25.0) MD: -7.27 (95% CI -14.97 to 0.44). *3 months post-allocation:* I: 50.3 (25.1) C: 61.8 (23.6) MD -11.49 (95% CI 21.82 to -1.16), (p<0.05). *6 months post-allocation:* I: 53.3 (26.5) C: 55.9 (26.4) MD -2.66 (-14.37 to 9.05), (ns).	to 3.67), (ns).	reported).	assessors blinded.
Langlais et al. 2017 [9] Canada	Study design: RCT Patient characteristics: Secondary provoked vestibulodynia. n=20. Mean age: 22 (range 18 to 27).	Intervention: Estrogen cream, topical self-administration of cream containing 0.3 mg of conjugated equine estrogen every night and after intercourse, for 8 weeks n=10. Control: Placebo cream n=10.	Pain during sexual intercourse, VAS (range 0-10), % reduction (95% CI) I: 27 (-1 to 55) C: 3 (-8 to 14) (p=0.29). Unadjusted RR for 10% improvement (95% CI): 1.40 (0.67 to 2.94).	FSFI, unadjusted RR for 10% improvement (95% CI): 1.33 (0.74 to 2.41).	Mild adverse events (pruritus): I: 0/10 (0%) C: 3/10 (30%).	Risk of bias Low Blinding: Patients and treatment providers blinded.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
		Follow-up time: Immediately post-treatment. Drop-out: I: 0/10 (0%) C: 0/10 (0%).				
Murina et al. 2013 [10] Italy	Study design: RCT, single centre. Patient characteristics: Provoked localized vulvodynia. n=20. Mean age: 28 (range 18 to 48).	Intervention: Oral palmitoylethanolamide (PEA) 400 mg+ transpolydatine 40 mg, twice daily for 60 days. n=10. Control: Placebo tablets n=10. Follow-up time: Immediately post-treatment. Drop-out: I: 0/10 (0%) C: 0/10 (0%).	Pain during intercourse, Marinoff dyspareunia scale (0-3) post treatment, mean (SD): I: 1.0 (0.9) C: 1.1 (0.9) (ns)		Serious adverse events: I: 0/10 (0%) C: 0/10 (0%). Mild adverse events (transient gastrointestinal symptoms): I: 2/10 (20%) C: 1/10 (10%).	Risk of bias: Moderate Blinding: Patients and treatment providers blinded. Comments: All patients received vaginal TENS therapy in a self-administered protocol 3 times each week.
Murina et al. 2018 [11] Italy	Study design: RCT, single centre. Patient characteristics: Provoked localized	Intervention: Diazepam, 5 mg, self-administration of one vaginal tablet every day for 60 days n=21.	Pain during intercourse, Marinoff dyspareunia scale (0-3) change from baseline. I: 0.9 C: 0.7 (p<0.01).		Serious adverse events: I: 0/21 (0%) C: 0/21 (0%). Mild adverse events,	Risk of bias: Low Blinding: Patients and treatment providers

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
	vulvodynia. n=42. Mean age: 29.0 (SD 7.8)	Control: Placebo tablet. n=21. Follow-up: Immediately post-treatment. Drop-out: I: 0/21 (0%) C: 0/21 (0%).			(drowsiness): I: 2/21 (10%) C: 0/21 (0%).	blinded. Comments: All patients had vaginal TENS therapy in a self-administered protocol 3 times each week.
Nyiresy et al. 2001 [12] USA	Study design: RCT, two centres. Patient characteristics: Provoked localized vulvodynia. n=34. Mean age: 27 (range 24 to 49).	Intervention: Cromolyn cream 4%, topical self-administration 3 times daily for 3 months n=16. Control: Placebo cream n=18. Follow-up time: Immediately post-treatment. Drop-out: I: 3/16 (%) C: 5/18 (%).	50% self-rated overall improvement: I: 5/13 (38%) C: 6/13 (46%) (ns). Decrease in symptoms of irritation, burning, and dyspareunia (range 0-3), mean (IQR): I: 0 (0-1) C: 1 (1-2) (ns).		Serious adverse events: I: 0/13 (0%) C: 0/13 (0%). Mild adverse events (stinging at application): I: 2/13 (17%) C: 0/13 (0%).	Risk of bias: Moderate Blinding: Patients, treatment providers and assessors blinded.
Petersen et al.	Study design:	Intervention:	Pain during sexual activity,	FSFI, mean (SD):	Serious adverse	Risk of bias:

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
2009 [13] Denmark	RCT, single-centre. Patient characteristics: Provoked vestibulodynia. n=65. Mean age: 30 (SD 6).	Botulinum toxin A, 20 units injected in the Bulbospongiosus muscle at one occasion. n=33. Control: Placebo injection (saline). n=32. Follow-up time: 6 months post-treatment. Drop-out: I:4/33 (12%) C: 1/32 (3%).	patients with ≥2 VAS point reduction: I: 14/29 (44%) C: 16/31 (50%) (p=0.893). VAS (0–10), mean (SD): I: 5.14 (1.53)* C: 5.13 (1.53)*. VAS change from baseline, difference between groups: Cohen's d=0 (p=0.98).	I: 18.46 (9.27), n=24 C: 20.34 (6.69), n=21 (ns). SF-36: (ns, data not reported in numbers).	events: I: 0/29 (0%) C: 0/31 (0%). Mild adverse events: I: 4/29 (14%) C: 2/31 (6%).	Low Blinding: Patients and treatment providers blinded. Comments: *SD pooled from I+C group.

BDI = Beck depression inventory (range 0-63, higher=worse); C = Control; CI = Confidence interval; FSFI = Female sexual function index (range 2-36, higher=better); I = Intervention; Index of sexual satisfaction (range 0-100, higher=better); IQR = Interquartile range; MD = Mean difference; MDS = Marinoff dyspareunia scale (range 0-3, higher=worse); MPQ = McGill Pain Questionnaire (range 0-78, higher=worse); OR = Odds ratio; PROMIS = Patient-Reported Outcomes Measurement Information System; RCT = Randomized controlled study: RR = Risk ratio; NRS = Numeric rating scale (range 0-10 or 0-100, higher=worse); NRSI = Non-randomized controlled study; State-Trait Anxiety Inventory of Spielberger (range 20-80, higher=worse); Standard deviation; TENS = Transcutaneous electrical nerve stimulation; VAS = Visual analogue scale (range 0-10 or 0-100, higher=worse).

All data have been extracted from the original studies unless otherwise stated. P-values represent comparisons between groups, as reported in the original study.

Table 2 Physiotherapy treatment.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
Danielsson et al. 2006 [14] Sweden	Study design: RCT, two centres. Patient characteristics: Provoked vestibulodynia. n=46. Mean age: 25 (range 18 to 36).	Intervention: Electromyographic biofeedback, 3 professional-administered sessions + 3 daily 10-min self-administered sessions for 4 months n=23. Control: Lidocaine treatment, topical application of 2% or 5% ointment gel 5-7 times daily for 4 months n=23. Follow-up time: Immediately post-treatment, 6- and 12-months post-treatment. Drop-out: I: 5/23 (22%) C: 4/23 (17%).	Pain during sexual intercourse, VAS (range 0-100), median (IQR): *12 months post-treatment:* I: 65 (28-74) C: 42 (21-72) (ns). Pain at pressure assessed with vulvar-algesiometer, increase in pressure threshold (range 3-1000g). I: site A 45 g, site B 20 g C: site A 20 g, site B 10g (ns).	Sexual satisfaction, VAS 0-100 (higher=better), median (IQR): *12 months post-treatment:* I: 47 (25-55) C: 63 (25-77) (ns). Quality of life, joy of living VAS 0-100 (higher=better), median (IQR). *12 months post-treatment:* I: 69 (57-80) C: 64 (42-80) (ns).	Mild adverse events: I: Pain on insertion of the vaginal probe (numbers not reported), and one case of candida infection C: Stinging pain at application (numbers not reported).	Risk of bias: Moderate Blinding: No blinding.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
Hullender Rubin et al. 2019 [15] USA	Study design RCT, single centre. Patient characteristics: Provoked vestibulodynia. n=19 Mean age: 29 (range 19 to 45).	Intervention: Traditional acupuncture, manually needling on 5 points followed by manual and electrical stimulation, 18 sessions over 12 weeks. n=10. Control: Non-traditional acupuncture, 4 needles on nonspecific points and sham stimulation, 18 sessions over 12 weeks. n=9. Follow-up time: Post-treatment and 12 weeks post-treatment. Drop-out: I: 3/10 (30%) C: 2/9 (22%).	Pain during sexual intercourse, VAS (range 0-100), mean during study period (SD): I: 30.5 (2.3) C: 39.3 (3.0) (p=0.53). Vulvar pain assessed with cotton swab test, VAS (range 0-100), mean change from baseline (SD): *Post-treatment:* I: −23.9 (28.7) C: −25.9 (14.3) (ns). *12 weeks post-treatment* I: −18.5 (31.7) C: −31.4 (18.3) (ns).		Mild adverse events, number of events: I: 32 C: 36. Serious adverse events, number of events: I: 0 C: 0.	Risk of bias Moderate Blinding: Patients and data analysts blinded. Comments: Both groups were instructed to apply lidocaine cream 4 times daily.
Morin et al. 2020 [16] Canada	Study design: RCT, multicentre. Patient characteristics: Provoked	Intervention: Physical therapy treatment, 10 weeks of individual 1-hour sessions including education, pelvic floor muscle exercises with	Pain during sexual intercourse, NRS (range 0-10), MD between groups (95% CI): *Post-treatment* 1.8 (1.2 to 2.3).	FSFI (range 2-36), MD between groups (95% CI): *Post-treatment* -4.4 (-6.1 to -2.7) n=201, p<0.001.	Serious adverse events: I: 0/99 (0%) C: 0/103 (0%). Mild adverse events:	Risk of bias: Moderate Blinding: Assessors blinded.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
	vestibulodynia. n=212. Median age: 22 (IQR 21 to 26).	biofeedback, manual therapy, and dilation. n=105. Control: Lidocaine treatment, topical overnight application of 5% ointment cream every night for 10 weeks. n=107. Follow-up time: Immediately post-treatment and 6 months post-treatment. Drop-out: I: 11/105 (10%) C: 6/107 (6%).	n=201, p<0.001. *At 6 months:* 1.8 (1.2 to 2.5), n=195, p<0.001.	*At 6 months:* -3.3 (-5.0 to -1.6), n=195, p<0.001.	I: 0/99 (0%) C: 16/103 (16%).	
Murina et al. 2008 [17] Italy	Study design: RCT, single centre. Patient characteristics: Provoked vestibulodynia. n=20. Mean age:	Intervention: Transcutaneous electrical nerve stimulation, 20 sessions of 30 min over 10 weeks. n=20. Control: Sham treatment (nonactive electrical stimulation), 20	Pain during sexual intercourse, MDS (range 0-3), mean (SD): *Post-treatment:* I: 1.1 (0.9) C: 2.4 (0.8). *3 months post-treatment:* I: 1.1 (0.9) C: 2.4 (0.8).	FSFI (range 2-36), mean (SD): *Post-treatment:* I: 25.3 (7.5) C: 17.8 (5.9). *3 months post-treatment:* I: 20.3 (7.5) C: 16.8 (5.9).	Adverse events: Not reported.	Risk of bias: Low Blinding: Patients blinded.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
	28 (range 21 to 44).	sessions of 30 min over 10 weeks. n=20. Follow-up time: Immediately post-treatment and 3 months post-treatment. Drop-out: I: 0/20 (0%) C: 0/20 (0%).				

BDI= Beck depression inventory (range 0-63, higher=worse); C=Control; CI=Confidence interval; FSFI=Female sexual function index (range 2-36, higher=better); I=Intervention; Index of sexual satisfaction (range 0-100, higher=better); IQR = Interquartile range; MD=Mean difference; MDS= Marinoff dyspareunia scale (range 0-3, higher=worse); MPQ=McGill Pain Questionnaire (range 0-78, higher=worse); OR=Odds ratio; PROMIS= Patient-Reported Outcomes Measurement Information System; RCT= Randomized controlled study: RR=Risk ratio; NRS=Numeric rating scale (range 0-10 or 0-100, higher=worse); NRSI= Non-randomized controlled study; Standard deviation; TENS=transcutaneous electrical nerve stimulation; VAS=Visual analogue scale (range 0-10 or 0-100, higher=worse);

All data have been extracted from the original studies unless otherwise stated. P-values represent comparisons between groups, as reported from analyses in the original study.

Table 3 Psychological treatment.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
Bergeron et al. 2001 [18] Canada Bergeron et al. 2008 [19] Canada	Study design: RCT comparing three interventions. Patient characteristics: Provoked vestibulodynia. n=87. Mean age: 26.8 years (SD 5.4).	Intervention 1: Group cognitive-behavioural therapy, (GCBT). Eight 2-hour groups sessions over a 12-week period. Intervention 2: Biofeedback, eight 45-minute sessions over a 12-week period. Biofeedback training involved self-insertion of a small sEMG sensor in the vagina. Intervention 3: *Vestibulectomy* (excision of the vestibular area to a depth of 2 mm and a width of 1 cm, all the way up to the urethra). Follow-up time: Immediately post-treatment and 6 months post-treatment (Bergeron 2001, [18]). 2.5 years post-treatment (Bergeron 2008, [19]).	Vestibular pain index assessed with cotton swab test, NRS 0-10. *Posttreatment, mean (SD)* GCBT 5.26 (2.00) Biofeedback 4.55 (2.36) Vestibulectomy 1.89 (1.68). Vestibulectomy had significantly lower posttreatment pain compared to GCBT ($p<0.01$) and biofeedback ($p<0.01$). *6 months, mean (SD)* GCBT 3.89 (2.09) Biofeedback 4.42 (2.63) Vestibulectomy 1.90 (2.24). Vestibulectomy had significantly lower pain compared to biofeedback ($p<0.05$) at 6 months. *2.5 years, mean (SD)* GCBT 3.66 (2.33) Biofeedback 4.22 (2.54) Vestibulectomy 1.58 (1.91) Vestibulectomy had significantly lower pain compared to GCBT ($p<0.01$) and biofeedback ($p<0.01$) at	Global sexual functioning (sexual history form, range 0-1). *Posttreatment, mean (SD)* GCBT 0.49 (0.12) Biofeedback 0.51 (0.08) Vestibulectomy 0.49 (0.14). *6 months, mean (SD)* GCBT 0.48 (0.11) Biofeedback 0.48(0.08) Vestibulectomy 0.45 (0.15). *2.5 years, mean (SD)* GCBT 0.46 (0.12) Biofeedback 0.48 (0.10) Vestibulectomy 0.43 (0.11).	Adverse events Not reported.	Risk of bias: Moderate for both studies. Blinding: No blinding. Comments: Drop out at 2.5 year follow up calculated on ITT population.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
		Drop-out at 6 months: I 1: 1/29 (3%) I 2: 1+2+8/29 (38%) I 3: 7+3/29 (35%). Drop-out 2.5 years: I 1: 10/29 (35%) I 2: 12/29 (41%) I 3: 14/29 (48%).	2.5 years. *Self-reported pain* (intensity of painful intercourse, NRS 0-10). *Posttreatment, mean (SD)* GCBT 6.00 (2.13) Biofeedback 5.43 (2.36) Vestibulectomy 3.93 (3.25). *6 months, mean (SD)* GCBT 4.46 (2.47) Biofeedback 4.50 (2.63) Vestibulectomy 3.41 (3.17). *2.5 years, mean (SD)* GCBT 3.30 (2.73) Biofeedback 4.29 (2.66) Vestibulectomy 2.05 (1.87).			
Bergeron et al. 2016 [20] Canada	Study design: RCT comparing two interventions. Patient characteristics: Provoked vestibulodynia. n=97. Mean age: 26.7 years (SD 6.1).	Intervention 1: Group cognitive-behavioural therapy (GCBT), 10 two-hour sessions over a 13-week period. n=52. Intervention 2 (Control): Topical steroid (twice daily application of 1% hydrocortisone cream) + written education materials about provoked vestibulodynia.	Pain during intercourse, (NRS 0-10), mean (SD). *Post treatment:* GCBT 5.46 (2.75) Topical steroid 5.67 (3.32) (p=0.55). *6 months:* GCBT 5.21 (2.87) Topical steroid 5.87 (3.07) (p=0.70).	FSFI (2-36, higher better functioning), mean (SD): *Post treatment:* GCBT 23.03 (7.59) Topical steroid 22.53 (7.63). (p=0.26). *6 months:* GCBT 22.33 (7.75) Topical steroid 23.30 (7.20) (p=0.63).	Adverse events: Not reported.	Risk of bias: Moderate Comments: Pain during intercourse was assessed only in those (n=92 at baseline) who were sexually active.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
		n=45. Follow-up time: Immediately post treatment, 6 months post-treatment. Drop-out: I: 17/52 (33%) C:16/45 (33%).				
Brotto et al 2019 [21] Canada Brotto et al. 2020 [22] Canada	Study design: Quasi-randomized clinical trial (47 participants were randomized and 83 were assigned non-randomly according to scheduling logistics). Patient characteristics: Provoked vestibulodynia. n=130. Mean age: 32 (SD 8).	Intervention: Mindfulness-based cognitive therapy (MBCT), 8 weekly group sessions of 2.25 h+ mindfulness home exercises n=67. Control: Cognitive behavioural therapy (CBT), 8 weekly group sessions of 2.25 h+ home exercises. n=63. Follow-up time: Post-treatment, 6- and 12-months post-treatment. Drop-out: *At 6 months (Brotto 2019,*	Pain during intercourse, NRS (range 0-10), mean (SD): *Post-treatment:* I: 4.34 (2.22) C: 4.65 (2.21) (p=0.03). *6 months post-treatment:* I: 3.39 (1.89) C: 4.03 (2.11) (p=0.02). *12 months post-treatment:* I: 3.62 (3.09) C: 3.97 (2.51) (p=0.53). Vulvar pain assessed with vulvalgesiometer (range 0-10), mean (SD): *Post-treatment:* I: 3.21 (1.96) C: 3.60 (2.14)	FSFI (range 2-36), mean (SD): *Post-treatment:* I: 21.79 (6.83) C: 23.41 (5.72) (p=0.72). *6 months post-treatment:* I: 24.75 (5.62) C: 23.20 (5.45) (p=0.09).	Adverse events: Not reported.	Risk of bias: Moderate for both studies. Blinding: No blinding. Comments: Pain during intercourse was assessed only in those (n=98) who were sexually active.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
		[21]): I: 8/67(12%) C: 14/63 (22%). *At 12 months (Brotto 2020 [22]):* I: 23/67 (34%) C: 18/63 (29%).	(p=0.34). *6 months post-treatment:* I: 2.92 (2.31) C: 2.86 (1.89) (p=1.00). *12 months post-treatment:* I: 2.52 (1.78) C: 2.00 (1.66) (p=0.27).			
Goldfinger et al. 2016 [23] Canada	Study design: RCT Patient characteristics: Provoked vestibulodynia n=20 Mean age: 26 (range 10 to 56).	Intervention: CBT program including education and home exercises, 8 individual sessions of 1.5 h for 8-24 weeks. n=10. Control: Physical therapy program including education and home exercises, 8 individual sessions of 1.5 h for 8-24 weeks. n=10. Follow-up time: Immediately post-treatment	Pain during sexual intercourse, VAS (range 0-10), mean reduction (SD): *Post-treatment:* I: 2.60 (1.43) C: 2.70 (2.36) (ns). *6 months post-treatment:* I: 2.10 (1.37) C: 2.40 (2.63) (ns). Vulvar pain assessed with cotton swab test VAS (range 0-10) *Post-treatment:* I: 3.26 (2.69) C: 1.28 (1.05) (p=0.03).	FSFI (range 2-36), mean (SD): *Post-treatment:* I: 27.37 (4.61) C: 27.06 (4.25) (ns). *6 months post-treatment:* I: 29.69 (5.12) C: 24.29 (7.18) (ns).	Adverse events: Not reported.	Risk of bias Moderate Blinding: No blinding. Comments: Outcomes on questionnaire data was based on 19 participants. P-values represent between-group effects from mixed-model analyses of variance (ANOVAs).

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
		and 6 months post-treatment. Drop-out: I: 0/10 (0%) C: 0/10 (0%).	*6 months post-treatment:* I: 2.62 (2.88) C: 1.86 (2.22) (ns).			
Guillet et al. 2019 [24] USA	Study design: RCT comparing two interventions. Patient characteristics: Provoked vestibulodynia. n=31. Mean age: 32 (SD 7).	Intervention 1: Mindfulness-based group cognitive behavioural therapy (M-gCBT), weekly sessions à 2.5 h for 8 weeks. n=14. Intervention 2 (Control): Education support, 8 weeks of online education with 3 in-person group visits. n=17. Follow-up time: Immediately post treatment, at 3 and at 6 months post-treatment. Drop-out: I: 0/14 C: 0/17.	Tampon test (NRS range 0-10) Between group change, MD (95% CI). *Post intervention:* 0.022 (−1.27 to 1.32), p=0.97 *3 months:* −0.67 (−2.04 to 0.70), p=0.34. *6 months:* −0.56 (−1.95 to 0.83), p=0.43.	FSFI, between group change, MD (95% CI) *Post intervention:* 12.5 (0.66 to 24.34), p=0.039 *3 months*: 15.12 (3.38 to 26.87), p=0.012 6 months: 12.10 (−0.041 to 24.24), p=0.051. Generalized Anxiety Disorder 7 (GAD-7; range 0–21), MD (95% CI) *Post intervention:* −3.39 (−5.78 to −1.00), p=0.006 *3 months:* −2.31 (−4.75 to 0.12) p=0.063. *6 months:* −2.83 (−5.27 to −0.40) p=0.023. Depression Beck Depression Inventory: (BDI-PC; range 0–63). *Post intervention:* −2.04	Adverse events: Not reported.	Risk of bias: Moderate

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	**Results:** • Pain during intercourse • Pain at pressure	**Results:** • Sexual function/satisfaction • Quality of life • Anxiety • Depression	**Results:** • Adverse events	Risk of bias Blinding Comments
				(−6.64 to 2.55) p=0.38 *3 months:* −3.52 (−8.25 to 1.20), p=0.14 *6 months:* −5.01 (−9.84 to −0.18), p=0.042.		

BDI = Beck depression inventory (range 0-63, higher=worse); C = Control; CI = Confidence interval; FSFI = Female sexual function index (range 2-36, higher=better); GCBT = Group cognitive-behavioural therapy; I = Intervention; Index of sexual satisfaction (range 0-100, higher=better); MD = Mean difference; MDS = Marinoff dyspareunia scale (range 0-3, higher=worse); M-gCBT = Mindfulness-based group cognitive behavioural therapy; MPQ = McGill Pain Questionnaire (range 0-78, higher=worse); OR = Odds ratio; PROMIS = Patient-Reported Outcomes Measurement Information System; RR =Risk ratio; NRS = Numeric rating scale (range 0-10 or 0-100, higher=worse); SD = Standard deviation; sEMG = Surface Electromyography; TENS = Transcutaneous electrical nerve stimulation; VAS = Visual analogue scale (range 0-10 or 0-100, higher=worse);

All data including p-values have been extracted from the original studies. P-values represent comparisons between groups, as reported from analyses in the original study.

Table 4 Other treatments.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
Gruenwald et al. 2021 [25] Israel	Study design: RCT, single centre. Patient characteristics: Provoked vestibulodynia. n=34. Mean age: I: 27 years (SD 8) C: 25 years (SD 9).	Intervention: Low intensity shock wave therapy twice a week for 6 weeks. Each treatment consisted of 500 pulses of shockwaves (0.09 mJmm2) n=23. Control: Sham treatment given at same treatment protocol n=9. Follow-up time: 1- and 3-month post treatment. Drop-out: I: 1/24 (4%) C: 1/10 (10%).	Pain during sexual intercourse, VAS range 0-10, mean (SD). *1-month post-treatment:* I: 5.70 (2.3) C: 8.30 (1.6). *3 months post-treatment:* I: 4.4 (2.5) C: 7.90 (2.2). Pain threshold, assessed with algometer test as applied radial pressure (mmHg) for first pain sensation, mean (SD). *1-month post-treatment:* I: 34.7 (18.8) C: 26.9 (10.3). *3 months post-treatment:* I: 69.8 (11.8) C: 34.9 (35.1).	FSFI (range 2-36), mean (SD). *1-month post-treatment:* I: 20.9 (6.2) C: 21.9 (4.7). *3 months post-treatment:* I: 22.5 (8.0) C: 21.1 (5.1).	Mild adverse events: I: 1/23 (4%) (low abdominal pain) C: 0/9 (0%).	Risk of bias: Moderate
Lev-Sagie et al. 2017 [26]	Study design: RCT, single centre, with a blinded phase of 6 weeks and an unblinded	Intervention: Low-level laser therapy, non-thermal pulsed light irradiation at the vestibule,	Pain during sexual intercourse according to diary, NRS (range 0-10), change from baseline, mean (SD):	Satisfaction with overall sexual life, any inference, n/N, post-treatment: I: 59%	Adverse events: I: 0/18 C: 0/17.	Risk of bias: Moderate Blinding: Patients and

Author **Year** **Reference** **Country**	**Study design** **Patient characteristics**	**Intervention** **Control** **Follow-up time** **Drop-outs**	**Results:** • **Pain during intercourse** • **Pain at pressure**	**Results:** • **Sexual function/satisfaction** • **Quality of life** • **Anxiety** • **Depression**	**Results:** • **Adverse events**	**Risk of bias** **Blinding** **Comments**
Israel	phase (data only extracted from blinded phase). Patient characteristics: Provoked vestibulodynia. n=34. Mean age: 26 (range 19-46).	2 weekly sessions for 6 weeks. n=18. Control: Sham treatment given at same treatment protocol. n=17. Follow-up time: Immediately post-treatment. Drop-out: I: 0/18 (0%) C: 1/17 (6%).	I: 0.9 (1.94) C: 0.10 (1.99) (p=0.245). Vulvar pain assessed with cotton swab test, NRS (range 0-100), change from baseline, mean (SD): I: 6.3 (2.8) C: 7.0 (9.1) (p=0.954).	C: 87% (p=0.507).		treatment providers blinded.
Morin et al. 2017 [27] Canada	Study design: RCT, single centre. Patient characteristics: Provoked vestibulodynia. n=40. Mean age: 22 (IQR 20 to 24).	Intervention: Transcranial direct-current stimulation, 10 sessions of 20 minutes over 2 weeks. n=20. Control: Sham treatment at same treatment protocol. n=20. Follow-up time: Immediately post-treatment, and 3 months post-	Pain during sexual intercourse, VAS (range 0-10), change from baseline, mean (95% CI): *Post-treatment:* I: 1.2 (0.4 to 2.1) C: 1.8 (0.8 to 2.8) (p=0.84). *3 months post-treatment, difference between groups:* P=0.09.	FSFI (range, 2-36), mean (95% CI): *Post-treatment:* I: 23.9 (21.3 to 26.5) C: 22.2 (19.7 to 24.7) (p=0.35). *3 months post-treatment:* I: 23.4 (20.8 to 26.0) C: 23.9 (21.3 to 26.4) (p=0.79). STAI, state domain, mean (95% CI):	Adverse events, total number of events: I: 94 C: 73.	Risk of bias: Low Blinding: Patients, treatment providers and assessors blinded.

Author Year Reference Country	Study design Patient characteristics	Intervention Control Follow-up time Drop-outs	Results: • Pain during intercourse • Pain at pressure	Results: • Sexual function/satisfaction • Quality of life • Anxiety • Depression	Results: • Adverse events	Risk of bias Blinding Comments
		treatment. Drop-out: I: 1/20 (5%) C: 0/20 (0%).		*Post-treatment:* I: 35.2 (31.3 to 39.7) C: 32.8 (29.2 to 36.8) (p=0.39). *3 months post-treatment:* I: 34.0 (30.2 to 38.3) C: 30.0 (26.7 to 33.7) (p=0.14). BDI (range, 0-63), mean (95% CI): *Post-treatment:* I: 5.3 (3.5-7.9) C: 5.5 (3.7-8.1) (p=0.92). *3 months post-treatment:* I: 5.0 (3.4 to 7.5) C: 4.1 (2.8 to 6.1) (p=0.48).		

BDI= Beck depression inventory (range 0-63, higher=worse); C=Control; CI=Confidence interval; FSFI=Female sexual function index (range 2-36, higher=better); I=Intervention; Index of sexual satisfaction (range 0-100, higher=better); IQR = Interquartile range; MD=Mean difference; MDS= Marinoff dyspareunia scale (range 0-3, higher=worse); MPQ=McGill Pain Questionnaire (range 0-78, higher=worse); OR=Odds ratio; PROMIS= Patient-Reported Outcomes Measurement Information System; RCT= Randomized controlled study: RR=Risk ratio; NRS=Numeric rating scale (range 0-10 or 0-100, higher=worse); NRSI= Non-randomized controlled study; SD=Standard deviation; STAI=State-Trait Anxiety Inventory of Spielberger (range 20-80, higher=worse), TENS=transcutaneous electrical nerve stimulation; VAS=Visual analogue scale (range 0-10 or 0-100, higher=worse);

All data have been extracted from the original studies unless otherwise stated. P-values represent comparisons between groups, as reported from analyses in the original study.

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