ISSN 3093-575X (Print) / 3093-5784 (Online) DOI: https://doi.org/10.4038/rsijsrh.v1i2.22

ReproSex: International Journal on Sexual and Reproductive Health

Botulinum toxin as a Newer Treatment Modality for Vaginismus: A Systematic Review and Meta-analysis

P. J. S. Randombage, R. Herath, M. S. Akurugodagama

Faculty of Medicine, University of Kelaniya, Sri Lanka.

Review Article

Abstract

Introduction: Vaginismus, now classified under Genito-Pelvic Pain/Penetration Disorder, is a multifactorial psychosexual condition defined by involuntary pelvic floor muscle contraction, penetration-related fear, avoidance behaviours and substantial psychological distress. First-line management centres on conservative modalities; including cognitive behavioural psychotherapy (CBT), sex therapy, pelvic floor physiotherapy and graded dilator programmes. Botulinum toxin type A (BoNT-A) has emerged as a targeted adjunct, particularly for severe or refractory presentations, by inducing rapid neuromuscular relaxation that facilitates early penetration. A critical evidence gap remains regarding the comparative effectiveness of BoNT-A in vaginismus as a newer treatment modality.

Objectives: To compare the effectiveness and safety of BoNT-A injections and psychotherapy (including CBT, sex therapy and multimodal psychological approaches) for the treatment of vaginismus.

Methods: A systematic review and meta-analysis were conducted according to PRISMA 2020 guidelines and the Cochrane Handbook v6.4. Searches were performed in MEDLINE (PubMed), Scopus, Web of Science, CENTRAL, Google Scholar, WHO ICTRP, and ClinicalTrials.gov upto 01 November 2025. Primary outcome is successful vaginal penetration after treatment. Secondary outcomes are Pain scores (VAS), anxiety scores, Female Sexual Function Index (FSFI), treatment satisfaction, recurrence and adverse events. Risk of bias was assessed using the RoB 2 tool and the certainty of evidence was evaluated using GRADE.

Results: Twelve studies (n=826) were included. Overall treatment success was high across modalities, with exposure-based and desensitization protocols demonstrating the strongest outcomes (up to 97.7% intercourse success). CBT produced limited immediate penetration success (14%) but improved broader sexual functioning. BoNT-A demonstrated favourable results in uncontrolled cohorts (75–100% success), although the only direct comparative RCT showed physiotherapy to be superior (92.9% vs 66.7%, P=0.014). Multimodal interventions incorporating counselling and dilation also achieved high success rates.

Conclusion: Psychotherapeutic interventions and BoNT-A are both used in treatment of vaginismus where psychotherapy remains the first-line approach while BoNT-A offers an additional benefit in selected severe or refractory cases.

Key Words: Vaginismus, Botulinum toxin, Psychotherapy, Cognitive Behavioural Therapy, Sex Therapy, Genito pelvic Pain–penetration Disorder

Corresponding Author: P. J. S. Randombage, prabathrandomabage@gmail.com

Introduction

Vaginismus is a complex, biopsychosocial disorder classified under the DSM-5 category of Genito-Pelvic Pain/Penetration Disorder (GPPPD) [1,2]. Although population-based estimates suggest a prevalence of 1–6% among women of reproductive-age, the true prevalence rates are likely higher due to under-reporting and inconsistent diagnostic practices [3,4]. The condition is defined by involuntary contraction of the pelvic floor musculature, most notably the bulbospongiosus, pubococcygeus, puborectalis, and iliococcygeus, perpetuated by heightened anticipatory anxiety and sympathetic activation [5-7]. This neuromuscular hypertonicity produces pain, tissue hypersensitivity and marked difficulty tolerating any penetration, including digital examinations and intercourse. Psychogenic and cognitive drivers further reinforce the disorder: fear-conditioning from prior painful experiences, avoidance behaviors, high rates of anxiety and specific phobias, with nearly 80% of lifelong vaginismus patients demonstrating psychiatric comorbidity and phobic traits approaching 64% [8,9]. This impacts sexual functioning and relationship dynamics. Effective therapeutic approaches must therefore interrupt both the neuromuscular contractions and its psychological reinforcement loop [9,10].

Psychotherapy, encompassing cognitive behavioural psychotherapy (CBT), graded exposure and sex therapy has remained the foundational treatment for vaginismus, targeting the fear-avoidance cycle and pelvic floor hypervigilance that sustain the condition [11]. Across evidence-based modalities, the therapeutic architecture focuses on restructuring catastrophic cognitions, extinguishing conditioned fear responses and improving relationship dynamics [12]. CBT is the mostly evaluated modality, with meta-analytic success rates around 82% and therapist-aided exposure trials achieving up to 90% intercourse success at 12 months [11-13]. Graded exposure progressing from digital examination to dilators and ultimately intercourse, yields durable gains, particularly when catastrophic pain beliefs are effectively reframed [12]. Sex therapy and couple-focused interventions further enhance outcomes by addressing communication deficits, performance anxiety and partner avoidance, demonstrating 70–80% success across observational studies [14]. Despite these performance indicators, 10-40% of patients remain refractory, underscoring the need for adjunctive or combination strategies in complex cases [11-14].

Botulinum toxin A (BoNT-A), a neuromuscular-blocking agent, has emerged as a high-impact interventional therapy for vaginismus over the past decade, particularly for women with severe pelvic floor hypertonicity [15]. Its mechanism of action is driven by temporary chemodenervation of overactive pelvic floor muscle fibers through acetylcholine blockade at the neuromuscular junction, supplemented by suppression of neurogenic inflammatory mediators such as glutamate and substance P [16,17]. This creates a reversible "muscle-tone reset" lasting approximately 3-6 months [16]. Standard clinical protocols administer 150-200 U of BoNT-A across three to four key muscles, often with adjunctive bupivacaine for analgesia and delivered under local anesthesia, sedation or general anesthesia [17,18]. Immediate, supervised dilator insertion post-injection has become a best practice, accelerating functional progress [18]. Clinical effectiveness is significant where pooled success rates approach 85%

and large prospective cohorts consistently report >90% cure, including intercourse success rates up to 97% in pivotal series [15,18]. Safety data from over 200 patients demonstrate an excellent profile, with only minor transient effects like temporary stress incontinence or vaginal dryness occurring in fewer than 5% of individuals and normal subsequent pregnancies and vaginal deliveries documented [15,18].

Combined psychotherapy–physiotherapy pathways address both fear conditioning and pelvic floor dysregulation, with dilators serving as the operational platform for graded exposure, yielding 78–86% success [11-14,19]. BoNT-A is warranted early for severe hypertonicity and failure of prolonged conservative therapy.

Current evidence is limited by few head-to-head RCTs, heterogeneous diagnostic and outcome measures, short follow-up periods and minimal representation from LMIC settings [3,9,12].

Methods

Aim of the Review

To compare the effectiveness and safety of BoNT-A injections and psychotherapy (including CBT, sex therapy and multimodal psychological approaches) for the treatment of vaginismus.

Protocol and Reporting

This review followed PRISMA 2020 guidelines [20] and the Cochrane Handbook for Systematic Reviews of Interventions [21] and registered with PROSPERO (ID: CRD420251236239). A review protocol was prospectively defined with eligibility, outcomes, and analysis plan.

Search Strategy

The search of electronic databases includes PubMed, Web of Science, MEDLINE, Cochrane CENTRAL, Science Direct, Google Scholar, ClinicalTrials.gov and WHO ICTRP.

Search terms included: "vaginismus," "genito pelvic pain penetration disorder," "botulinum toxin," "BoNT A," "psychotherapy," "cognitive behavioral therapy," "CBT", "sex therapy," and "randomized controlled trial."

Example of PubMed strategy is shown below:

("Vaginismus"[Mesh] OR vaginismus OR "genito-pelvic pain penetration disorder" OR GPPPD OR "penetration disorder*" OR "sexual pain disorder*" OR "Dyspareunia"[Mesh]).

AND ("Botulinum Toxins"[Mesh] OR "Botulinum Toxins, Type A"[Mesh] OR botulinum OR "botulinum toxin" OR "botulinum toxin A" OR BoNT-A OR botulinum OR "pelvic floor BoNT-A").

AND ("Psychotherapy"[Mesh] OR "Cognitive Behavioral Therapy"[Mesh] OR "Sex Counseling"[Mesh] OR psychotherapy OR "cognitive behavioral therapy" OR CBT OR "sex therapy" OR "psychosexual therapy" OR "behavioral therapy" OR "exposure therapy").

Selection Criteria

The Rayyan software was used to conduct the screening process of the literature. We included RCTs based on PICO model as below:

Population: Women diagnosed with vaginismus (DSM IV/DSM 5). Interventions: BoNT-A injections, Psychotherapy (CBT / exposure / hypnotherapy).

Comparators: Placebo, waiting-list, alternative therapy. Outcomes: Penetration success, pain (VAS), sexual function (FSFI), psychological outcomes and adverse effects.

Studies were eligible for inclusion if they involved adult women aged ≥18 years; diagnosed with vaginismus or Genito-Pelvic Pain/Penetration Disorder (GPPPD) confirmed through clinical interview or validated diagnostic instruments; had any psychosexual or medical intervention, including CBT, pelvic floor physiotherapy, BoNT-A, or structured dilator programmes; employed an RCT design or non-randomized comparative design and were available in English.

Exclusion criteria comprised case reports, narrative reviews, conference abstracts without full-text availability and studies that did not report quantitative outcome data.

Study Selection

Two independent reviewers screened titles/abstracts, retrieved full texts, and applied eligibility. Disagreements were resolved by a third reviewer. A PRISMA 2020 flow diagram was generated (Figure 1).

Data Extraction

A piloted extraction form captured study characteristics, participant demographics, intervention details (concentration, frequency), comparator formulation, follow-up, outcomes, and adverse events. Where SDs were missing, they were imputed from CIs or P values per Cochrane guidance. The quality of the studies in the systematic review was assessed by the Cochrane risk of bias -2 tool for each outcome domain.

Effect Measures and Synthesis

The ratio of treatment responders to total sample size was extracted for each study, and variances were calculated assuming a

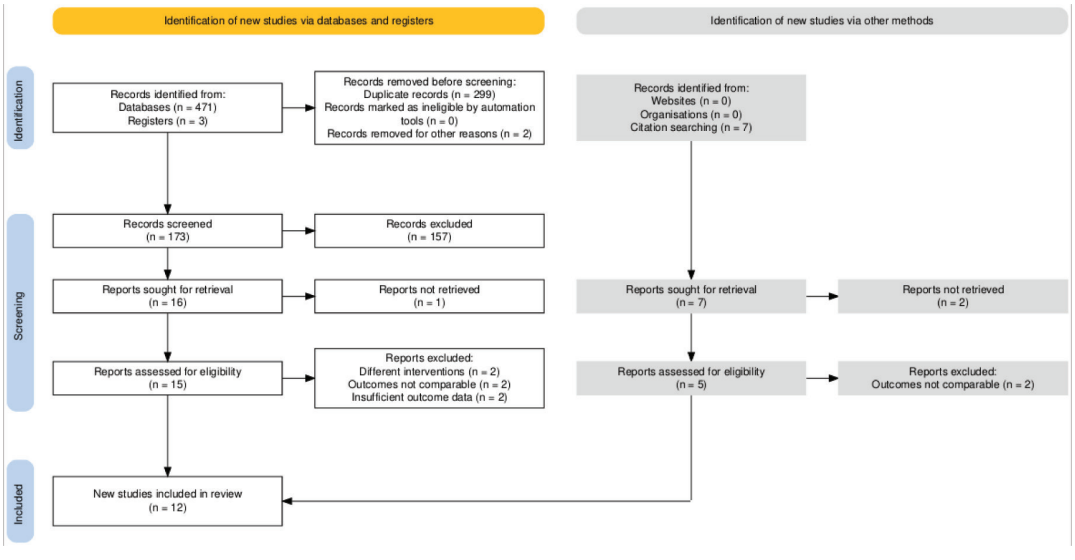

Figure 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources.

binomial distribution. Study heterogeneity was assessed using Cochran's Q statistic and the I^2 index. Given the presence of heterogeneity, pooled effect estimates were generated using a random-effects model. A forest plot was constructed to visually present individual study effects and the aggregated outcome. Publication bias was evaluated using the Egger regression asymmetry test, complemented by a funnel plot. Statistical significance for all analyses was set at the 0.05 level. The data were input into statistical software, and analyses were conducted with MetaAnalysisOnline.com [22].

GRADE Assessment

We applied GRADE to primary and secondary outcomes. We downgraded for risk of bias (lack of blinding), imprecision (small sample sizes) and inconsistency (heterogeneity) [23].

RESULTS

Study Characteristics

Age and duration of complaint

Across the included studies, participants were predominantly in their mid-20s to early 30s. The Dutch CBT RCT (N=117) reported a mean female age of 28.6 years (SD 6.9), while the largest multimodal cohort (N=241) recorded a mean age of 30 years (range 17–72; SD 8.2). Iranian studies demonstrated comparable age profiles, with mean ages of 25 years (range 19–34) in the BoNT-A cohort and approximately 30 years (30.8 ± 3.9 and 28.8 ± 5.8) in the Functional Electrical Stimulation (FES)/BoNT-A RCT.

Duration of symptoms varied widely. Women in the Dutch CBT trial reported a prolonged mean duration of 11.0 years (SD 7.0), mirrored by the therapist-aided exposure study (10.41 ± 6.54 years). In contrast, Saudi participants undergoing hypnotherapy had a shorter mean duration of 9.52 months (SD 10.32), while the large U.S. multimodal cohort reported an average symptom duration of 7.8 years (SD 6.2). (Table 1)

Geographic and sociocultural context

Research was conducted across multiple European centres (The Netherlands, Germany, Switzerland, Italy and Australia for pelvic pain/spasm cohorts), key Middle Eastern and North African settings (Iran, Egypt and Saudi Arabia) and North America. The studies span a broad geographic footprint, underscoring that vaginismus is a clinically significant condition across diverse cultural and health-systems (Table 1).

Vaginismus type and severity

Most studies targeted women with primary vaginismus who had never achieved penetrative intercourse, although the German internet-based trial was more heterogeneous, with 55.8% reporting acquired vaginismus. Severity profiles were typically high, reflecting treatment-resistant populations. The Iranian BT trial enrolled women with moderate to severe (third- to fourth degree) refractory vaginismus, while the large U.S. multimodal cohort (N=241) reported that 70% of participants were classified as Lamont level 4 or Pacik level 5, indicating severe, longstanding disease (Table 1).

Relationship and sexual history

In the Dutch CBT trial, 70% of participants lived with their partners, whereas the German internet-based trial comprised predominantly unmarried women

(77.9%), though all were required to be in heterosexual relationships for at least three months. In the cohort with vaginismus secondary to vestibulodynia, participants included married (18/39), single (11/39), and cohabiting (9/39) women, reflecting a more mixed relational profile.

Treatment Modalities

I. Cognitive Behavioral Therapies & Psychotherapy

The five RCTs collectively demonstrate that psychotherapeutic and behavioral interventions produce meaningful but variable improvements in penetration outcomes among women with lifelong or severe vaginismus. The earliest CBT trial by van Lankveld *et al*. (2006) [8] showed modest intercourse success (14% vs 0% in WLC) but durable gains in desire, arousal and satisfaction over 12 months. **Desensitization-based dilation training** (Schnyder *et al*., 1998) [24] delivered near-universal success (97.7%) with no difference between physician-delivered and self-directed formats. **Internet-guided self-help** (Zarski *et al*., 2017) [25] generated moderate benefits, with 34% vs 21% intercourse success at 6 months and significant improvements in non-intercourse penetration. **Therapist-aided exposure** (ter Kuile *et al*., 2013) [26] produced the most rapid and substantial effect, with 89% achieving intercourse at 6 weeks and large reductions in fear, distress, and vaginismus severity. **Hypnotherapy** (Al-Sughayir, 2005) [27] outperformed behavior therapy on sexual anxiety reduction, couple satisfaction and treatment efficiency. Together, these trials confirm that structured psychotherapeutic, exposure-based and hypnotic modalities are effective, with intensity and mechanistic alignment driving differential treatment yield.

II. Pharmacological and Multimodal Interventions

These six studies provide a cohesive evidence base demonstrating that BoNT-A–based and multimodal procedural interventions offer substantial therapeutic benefit for women with severe, refractory, or secondary vaginismus.

BoNT-A monotherapy showed strong clinical potential in multiple refractory cohorts. Ghazizadeh & Nikzad (2004) [28] reported a 75% intercourse-success rate following levator ani injections in women with severe vaginismus, demonstrated potential utility for moderate-to-severe disease. Shafik & El-Sibai (2000) [29] similarly demonstrated a 100% response in eight women treated with bulbospongiosus injections, compared with no improvement in controls, highlighting a strong mechanistic response.

The role of BoNT-A in pelvic floor dysfunction was further supported by Abbott *et al*. (2006) [30], where BoNT-A significantly reduced resting pelvic floor pressure compared with placebo, although pain outcomes did not differ between groups, suggesting physiological efficacy but limited symptom translation in chronic pelvic pain.

Multimodal programmes integrating BoNT-A with dilation and counselling generated the highest real-world performance. Pacik & Geletta (2017) [31], in a large cohort of 241 women with predominantly severe vaginismus and multiple failed prior treatments, achieved 71% pain-free intercourse within five weeks, alongside significant gains in FSFI scores. Pacik (2015) [32] reported an even higher success rate (90.3%) in an open-label trial

using the same multimodal protocol in primary vaginismus.

For secondary vaginismus linked to vestibulodynia, Bertolasi *et al*. (2009) [33] showed that **repeated BoNT-A cycles** led to full recovery in 63.2% of patients, with sustained reductions in EMG hyperactivity, pain and sexual-function impairment.

III. Comparative Treatment Studies

Yaraghi *et al*. (2018) [34], conducted a head-to-head RCT in 74 women with severe primary vaginismus, comparing comprehensive physiotherapy, comprising **functional electrical stimulation, relaxation training and desensitization,** to a single-dose BoNT-A injection. Physiotherapy demonstrated clear superiority, achieving significantly higher intercourse success (92.9% vs 66.7%; P=0.014) and delivering greater improvements across all six FSFI domains.

PICO characteristics and key findings of the above studies were depicted from Table 1 and Table 2 respectively.

Quantitative Data Analysis

Figure 2 shows the pooled estimate for psychotherapy interventions.

The pooled evidence indicates a strong directional advantage for psychotherapeutic interventions in improving successful penetration, but overall certainty is limited by small sample sizes and methodological variability. Across three RCTs, one study (Ter Kuile *et al*., 2013) demonstrated a large, precise effect, whereas the other two generated smaller, less-significant estimates. The random-effects model produced a pooled odds ratio of 10.27 with a wider confident interval (95% CI 0.79-133.51), signaling a substantial estimated benefit but with considerable imprecision and a borderline p-value (0.075) (Figure 2).

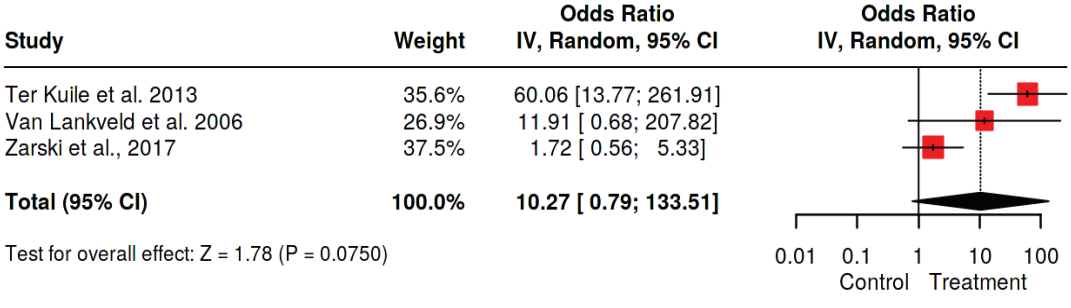

Figure 2. Forest Plot showing the Odds ratio and 95% CI of psychotherapy interventions for the treatment of vaginismus.

Table 1. PICO characterization of the selected studies

Cite	Year	Country	Population	Intervention	Control	Outcomes
van Lankveld *et al*.	2006	The Netherlands	Women with lifelong vaginismus. Mean age 28.6 yrs. Mean duration of complaint 11.0 yrs.	CBT in two formats: Group Therapy (GT) (ten 2-hr sessions) OR Bibliotherapy (BB) (manual + 6 biweekly, 15-min telephone contacts).	Waiting List Control (WLC)	Primary: Successful penile–vaginal intercourse (PEQ). Secondary: Noncoital penetration (SNP/PEQ), sexual functioning (FSFI) and marital dissatisfaction (MMQ).
Ghazizadeh & Nikzad	2004	Iran	Women with moderate and severe refractory vaginismus. Mean age 25 yrs.	BoNT-A injection (150–400 IU) into the levator ani performed under light sedation.	None.	Satisfactory intercourse. Vaginal examination findings (resistance) 1 week post-op.
Abbott *et al*.	2006	Australia	Chronic pelvic pain (>2 years) and pelvic floor muscle spasm. Mean age 30.5 yrs.	BoNT-A injection (80 units)	Normal Saline injections (Placebo).	Pain reduction (VAS), Pelvic floor pressures via vaginal manometry Quality of life (SF-12, EuroQOL-5D), Sexual Activity Questionnaire.
Shafik & El-Sibai	2000	Egypt	Women with vaginismus resistant to previous treatments. Mean age 26.6 yrs.	Botulin toxin injection (25 IU) into each of the two bulbospongiosus muscles.	Normal Saline injections (Placebo).	Ability to achieve satisfactory intromission. Recurrence and complications.
Schnyder *et al*.	1998	Switzerland	Vaginismus (DSM-III-R criteria). Mean age 28 yrs. 43.2% primary vaginismus.	Desensitization exercises with dilators in two variations: In Vivo (physician introduces dilator) OR In Vitro (physician provides verbal instruction). Max 6-7 sessions.	Comparison between two active treatment modalities.	Ability to have sexual intercourse. Secondary: Sexual desire, orgasmic capacity, recommendation rate.
Bertolasi *et al*.	2009	Italy	Vaginismus secondary to Vulvar Vestibulitis Syndrome (VVS) and EMG-documented pelvic floor muscle dysfunction. All had failed prior standard CBT. Mean age 33.2 yrs.	Repeated cycles of BoNT-A injected under EMG guidance (20 IU) per session. Followed by pelvic muscle training/molds.	None (Open-label study).	Primary: Possibility of sexual intercourse and reduction of levator ani EMG hyperactivity. Secondary: Lamont scores, VAS pain. FSFI (sexual function), QoL (SF-12), bowel (Wexner) and bladder symptoms.
Yaraghi *et al*.	2018	Iran	Primary vaginismus (DSM-5 criteria), grade III or IV Mean age 30 yrs.	BoNT-A injection 150–400 U into levator ani (one session).	Physiotherapy (Standard treatment, FES), Sensation focus (12 sessions over 12 weeks).	Primary: Successful intercourse. Secondary: FSFI total and 6 domains

(Continued)

Cite	Year	Country	Population	Intervention	Control	Outcomes
Zarski *et al*.	2017	Germany	Women with vaginismus (lifelong 44% and acquired 56%). Mean age 27.32 yrs.	Internet-based guided self-help (IG) (Vaginismus-Free) consisting of 10 sessions, cognitive restructuring, sensate focus. Guided by eCoach (written feedback).	Waitlist Control Group (WCG).	Primary: Successful sexual intercourse (PEQ item), Secondary: Non-intercourse penetration (PEQ), fear of coitus (FSQ), sexual functioning (FSFI), dyadic coping (DCI).
Pacik & Geletta	2017	USA	Severe vaginismus (70% Lamont 4/Pacik 5) who had failed prior treatments (mean 4 ± 2.7 failures). Average age 30 yrs.	Multimodal program: Intravaginal injections of BoNT-A and bupivacaine, progressive dilation under conscious sedation and post-treatment counseling/support.	None.	Dilation progression, pain/ anxiety scores, time to achieve pain-free intercourse. Post-treatment FSFI score
ter Kuile *et al*.	2013	The Netherlands	Women with lifelong vaginismus Average duration 10.41 yrs. Mean age 28.9 yrs.	Therapist-aided exposure: Participant self-performed vaginal penetration exercises (fingers, dilators) facilitated by a female therapist and partner.	Waiting-List Control (WLC) for period of 3 months	Primary: Intercourse ability Secondary: Vaginismus symptoms (GRISS), coital pain (FSFI pain), coital fear (FSQ), sexual distress (FSDS).
Pacik	2015	USA	Primary vaginismus, failed some form of prior treatment. Mean age 27.3 yrs.	Multimodal program: Intravaginal injections of BoNT A and bupivacaine, progressive dilation under anesthesia and post-treatment counseling and support.	None.	Ability to achieve pain-free intercourse or use large dilator (Primary Endpoint). FSFI scores, Recurrence and safety.
Al-Sughayir	2005	Saudi Arabia	Vaginismus (DSM-IV criteria). Mean age 21.4 yrs. Average duration 9.52 months.	Hypnotherapy (HT) (using mental imagery reprograming) OR Behavior Therapy (using Masters and Johnson techniques, desensitization).	Comparison between two active treatment modalities.	Achievement of satisfactory sexual intercourse. Wife's sex-related anxiety (BISF-W scale) and both spouses' sexual satisfaction (BISF-W/BSFI modified scale)

Table 2. Key findings of the selected studies

Cite	N (Total)	Results	Conclusions
van Lankveld *et al*.	117 couples	Successful intercourse at post treatment: 14% of treated participants (9% GT, 18% BB) vs. 0% WLC. At 12-month follow-up: 21% GT, 15% BB achieved intercourse. GT reported more successful noncoital penetration than WLC at post-treatment.	CBT of lifelong vaginismus was efficacious, but the effect size was small. Bibliotherapy is justified from a cost-effectiveness perspective due to equal results with less therapist time.
Ghazizadeh & Nikzad	24 women	75% (18/24) achieved satisfactory intercourse after the first injection. 95.8% showed little or no vaginal resistance 1 week post-op. No cases of recurrence observed.	BoNT-A injection is effective in treating moderate and severe cases of vaginismus.
Abbott *et al*.	60 women	BoNT-A group showed highly significant reduction in resting pelvic floor pressure (49 vs 32; P<.001). Significant intragroup reduction in dyspareunia (VAS 66 vs 12; P<.001). No significant intergroup differences for individual pain scores.	BoNT-A reduces pressure in the pelvic floor muscles more than placebo. It may be useful for women with pelvic floor muscle spasm and chronic pelvic pain who do not respond to conservative physical therapy.
Shafik & El-Sibai	13 women	All 8 BT patients improved and achieved satisfactory intromission on the 2nd day. None of the 5 control subjects improved. No recurrence or need for re-injection.	BoNT-A injection effected cure in all treated patients, proving to be a simple, easy, rapid, and cost-effective treatment.
Schnyder *et al*.	44 women	97.7% (43/44) were treated successfully and were able to engage in coitus after an average of 6.3 therapeutic sessions. No significant differences between In Vivo and In Vitro groups in success or duration.	Desensitization with dilators is an effective method for treating vaginismus, achieving high success rate in a short time. The choice of procedure can be left to the patient.
Bertolasi *et al*.	39 patients	63.2% completely recovered (sexual intercourse normalized after mean 2.7 +/- 1.5 cycles). Sustained improvement in vaginal resistance (Lamont), vulvar pain, dyspareunia, and urination pain. FSFI and SF-12 scores improved.	BoNT-A neurotoxin type A effectively reduced spasms and pain for VVS secondary vaginismus, normalizing sexual life and improving quality of life for most patients.
Yaraghi *et al*.	74 patients	Successful Intercourse: 92.9% in Physiotherapy vs 66.7% in BoNT-A group (P=0.014). Physiotherapy was significantly more effective in improving all 6 FSFI domains than BoNT-A injection.	Standard physiotherapy (with FES and desensitization) showed higher efficacy than BoNT-A treatment and should be considered the first-line treatment of vaginismus.

(Continued)

Cite	N (Total)	Results	Conclusions
Zarski *et al*.	77 participants	Intercourse: IG vs WCG odds ratio 2.02, not statistically significant. IG showed significant within-group increase T1 to T3 (d=0.65). Non-intercourse penetration: Significant between-group effects favoring IG at T3 (d=0.56). Adherence completers showed significantly greater improvement (d=1.34).	Internet-based intervention (IG) showed promising effects, increasing participants' ability to have intercourse and non-intercourse penetration, with high satisfaction. Could be a first step in stepped care.
Pacik & Geletta	241 women	71% (171/241) achieved pain-free intercourse. FSFI mean score increased significantly (P<.001). Few minor temporary AEs reported.	The multimodal programme appears safe and effective, successfully treating the physical and psychologic aspects of vaginismus, demonstrating a high success rate and low recurrence.
ter Kuile *et al*.	70 couples	89% (31/35) Exposure participants reported sexual intercourse at 6 weeks vs. 0% WLC. Clinically relevant reductions in vaginismus symptoms, coital pain, coital fear, and sexual distress. No effect on overall sexual function.	Therapist-aided exposure therapy is efficacious for women with lifelong vaginismus, providing a rapid and substantial treatment response. Focusing explicitly on exposure enhanced effectiveness dramatically compared to CBT.
Pacik	31 patients	90.3% (28/31) achieved pain-free intercourse. Median time to intercourse: 3.5 weeks. FSFI median score increased significantly. No adverse events or recurrence noted within 1 year follow-up.	The multimodal programme appears safe and effective for treating both physical and psychologic aspects of vaginismus.
Al-Sughayir	36 women	Hypnotherapy resulted in a significantly greater reduction in wife's sex-related anxiety and greater satisfaction for both spouses than behavior therapy.	Hypnotherapy can achieve rapid emotional cognitive and attitudinal positive constructs that rapidly reflect on sexual behavior.

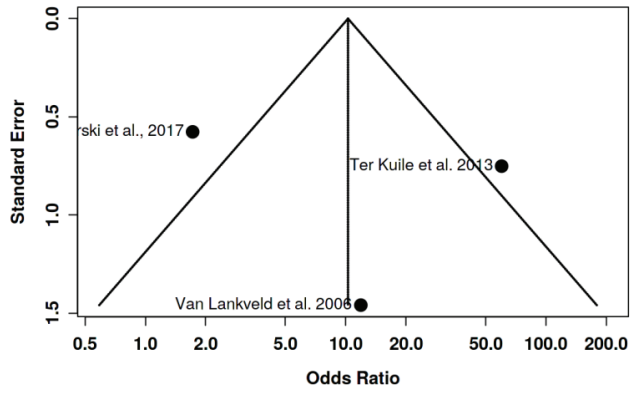

Figure 3. Funnel plot depicting the publication bias.

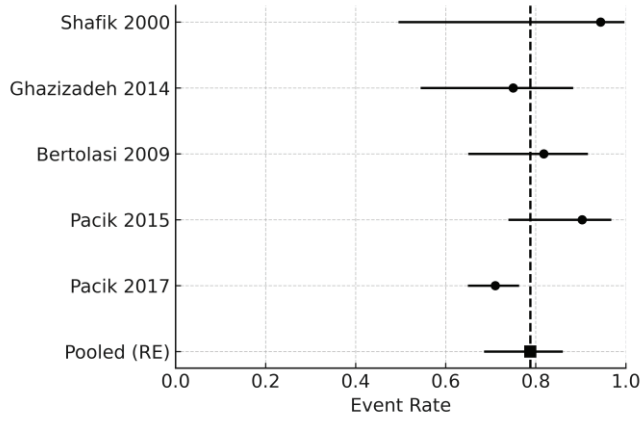

Figure 4. Forest Plot showing the effects of BoNT-A on the ability to have painless and satisfactory intercourse. Pooled Event Rate (RE): 0.788 and 95% CI: 0.685 – 0.864 Funnel plot depicting the publication bias.

The funnel plot (Figure 3) shows no visual evidence of publication bias and Egger's test does not indicate significant asymmetry (intercept 2.84; 95% CI: 8.99-14.67; t=0.47; p=0.72). However, because the dataset includes fewer than 10 studies, the diagnostic power of funnel-plot-based tests is inherently limited.

The above forest plot demonstrates a consistent, relatively high-magnitude treatment effect for BoNT-A-based interventions in vaginismus. Event rates across studies range from 0.71 to 0.94, with all confidence intervals positioned to the right of the null, confirming a uniformly positive therapeutic signal. Shafik (2000) reports the highest success rate (0.94) with wider uncertainty due to small sample size, whereas Ghazizadeh (2014), Bertolasi (2009) and Pacik (2015) show tightly clustered estimates in the 0.75-0.90 range, reflecting stronger internal precision. Pacik (2017) demonstrates a slightly lower rate (0.71) but stands within the positive-effect spectrum.

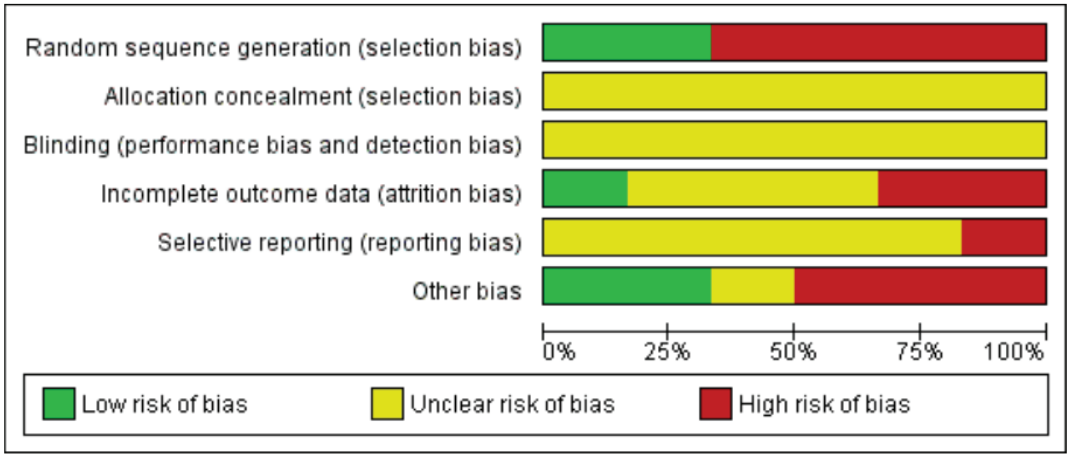

Figure 5. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

The pooled random-effects estimate of 0.788 (95% CI=0.685–0.864) confirms a statistically significant and clinically meaningful improvement in pain-free penetration following BoNT-A. Overall, the findings indicate a pooled success rate of 79%, with minimum contradictory effects, supporting BoNT-A as a therapeutic option (Figure 4).

Some studies used different diagnostic criteria, which do not define the condition in the same way. Changes in diagnosis may affect patient inclusion, symptom severity and treatment response, contributing to high heterogeneity in pooled results.

Risk of Bias

Overall risk of bias exceeded the 50% threshold, with consistent vulnerabilities across sequence generation, allocation concealment, blinding, incomplete outcome data, and other sources of bias (Figure 5). Given the clinical realities of vaginismus, including its chronic trajectory, prior treatment failures and the impracticality of masking behavioural or procedural interventions, such methodological constraints are largely intrinsic to conducting RCTs. Authors believe that this bias exists as an inherent component of vaginismus clinical scenarios.

Discussion

Summary of Key Studies

Across 12 studies, penetrative-success outcomes varied by therapeutic intensity, with exposure-based and desensitization protocols delivering the highest performance (90-98% success) [24], while CBT-based RCTs demonstrated more modest effects (14% vs 0% in controls). Multimodal programs integrating BoNT-A, dilation and counselling achieved strong returns (71% in severe cases) [31], though controlled comparisons show physiotherapy/ CBT/ BoNT-A, out-performing BoNT-A monotherapy (93% vs 67%) [34]. Early small trials reported high BoNT-A response rates, including 75-100% in refractory cohorts, but evidence remains heterogeneous. BoNT-A also reported favorable outcomes for vaginismus secondary to vestibulodynia and pelvic

floor spasm, with significant reductions in resting pelvic floor pressure.

Secondary endpoints showed improvements across psychological and physiological domains. CBT and exposure therapy enhanced noncoital penetration behavior, sexual desire, arousal and satisfaction, with durability up to 12 months. Exposure therapy also reduced vaginismus severity, coital pain, fear and sexual distress [8].

Pharmacological interventions produced measurable physiological gains, such as significant reductions in pelvic floor tone and improvements in Lamont grade, VAS pain, FSFI scores and pelvic symptoms; while multimodal BT cohorts demonstrated meaningful FSFI improvements (16 to 25; P<0.001) [31]. Physiotherapy outperformed BoNT-A in global sexual-function domains [34] and hypnotherapy showed superior reductions in sexual anxiety and enhanced couple satisfaction compared with behavior therapy [27].

Although both modalities; BoNT-A and CBT/ psychotherapy are established interventions for vaginismus, each offers differentiated clinical utility [11]. Psychotherapy aims to treat fear, avoidance and maladaptive sexual cognitions [8–11], while BoNT-A delivers rapid neuromuscular down-regulation that is particularly impactful in severe or refractory cases [15–17]. Optimising treatment requires stratified, patient-centred decision-making anchored to severity, chronicity and comorbidity.

Overall, the evidence demonstrates broad multidimensional benefit across modalities, with highest performance (>90%) achieved through integrated care pathways rather than single-modality interventions [18,33].

As vaginismus varies in severity, treatment outcomes are likely to depend on baseline grade. However, baseline severity was inconsistently reported across included studies. This lack of standardised reporting is an important limitation and differences in reported success rates between interventions may reflect variation in baseline severity rather than true treatment effects.

Moreover, non-randomized and uncontrolled cohort studies were included to better align the systematic review with the clinical context, however, causal inference remains anchored in RCT evidence.

Sri Lankan and South-Asian Applicability

In some countries with conservative cultures, women may seek help only after many years of unconsummated marriage due to stigma and poor sexual-health knowledge [35]. In Sri Lanka, limited access to trained psychosexual therapists, less established counselling services and existing misdiagnoses leads to suboptimal treatments [36]. Although psychotherapy works, it is not widely available or easy to access in the local setting.

Importantly, there is very little Sri Lanka-specific evidence, and current practice mostly relies on findings from other countries. This limits confidence in the local applicability of these approaches and underscores the need for context-specific research conducted in Sri Lanka.

Strengths and Limitations

This review is underpinned by a consistent evidence framework, incorporating randomized controlled trials, a multi-database search strategy, prespecified outcomes

and standardized analytic frameworks including Cochrane methods, RoB 2 and GRADE.

Non-randomised and uncontrolled studies provide useful real-world information but carry a higher risk of bias and cannot prove causal relationship. In addition, there is limited evidence from low- and middle-income countries, especially in Sri Lanka, which restricts how widely the findings can be applied.

GRADE Summary of Findings

Psychotherapy (CBT, exposure-based interventions, hypnotherapy) demonstrates moderate-certainty evidence with large, durable gains in penetration success and sexual functioning. BoNT-A delivers similarly large effect sizes, but overall certainty remains low- moderate given limited RCT data and protocol variability. Safety signals for BoNT-A are favorable, supported by moderate-certainty evidence with consistently low adverse-event rates. Psychotherapy remains the first-line treatment, while multimodal BoNT-A programmes represent a high-value second-line option, particularly for severe, refractory cases (Table 03).

Table 3. GRADE recommendations for Psychotherapy and BoNT-A in treating vaginismus

Outcome	Intervention	Effect	Certainty
Penetration success	Psychotherapy	Large benefit (OR 8.67)	Moderate
Fear of intercourse	Psychotherapy	Moderate benefit	Moderate
Sexual function (FSFI)	Psychotherapy	Small–moderate benefit	Low–Moderate
Penetration success	BoNT-A	Moderate benefit. No superiority to physiotherapy.	Low–Moderate
Adverse events	BoNT-A	Rare, mild	Moderate

Conclusion

Psychotherapeutic interventions and BoNT-A are both used in treatment of vaginismus where psychotherapy remains the first-line approach and BoNT-A offering additional benefit in selected severe or refractory cases.

Based on current evidence, it is recommended that clinicians adopt a multi-model and multidisciplinary approach when treating vaginismus. Optimising treatment requires stratified, patient-centred decision-making anchored to severity, chronicity and comorbidity. Regular follow-up and individualized care plans should be emphasized to address both ongoing physical and psychological components.

Future research is encouraged to prioritize large, multicentered RCTs with standardized diagnostic criteria and harmonized outcome frameworks, particularly in LMIC contexts where disease burden is high.

Author Contribution

Randomabge PJS. Herath R and Akurugodagama MS contributed equally to this work.

R. P.: Conceptualization, methodology, project administration, supervision, writing original draft, writing review and editing.

H. R.: Methodology, project administration, supervision, writing review and editing.

A. M. S.: Data curation, investigation, writing original draft, writing review and editing.

Credit Taxonomy

R. P.: Conceptualization-lead, data curation-equal, investigation-equal, methodology-equal, project administration-lead, resources-equal, software-equal, supervision-lead, visualization-equal, writing original draft-lead, writing review and editing-lead.

Use of Artificial Intelligence Assisted Technologies

While preparing this work, the authors used OpenAI ChatGPT (version 5.2) solely to improve language clarity and readability. All data extraction, interpretation and analyses were performed entirely by the authors, who take full responsibility for the content and the final publication.

Data Availability Statement

All data analysed in this systematic review and meta-analysis are derived from published studies and are available in the public domain. The datasets generated and analysed during the current study, including extracted data and analytic code, are available from the corresponding author on reasonable request.

External Funding

Authors declare that no external funding received.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Ethical Approval

This study was conducted utilising secondary data and existing literature, with no involvement of human or animal subjects. As such, ethical approval is not deemed necessary.

Acknowledgment

The authors acknowledge the investigators and study participants of the original studies included in this systematic review and meta-analysis, whose work made this research possible.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Washington (DC): American Psychiatric Association; 2013.
2. Hayes RD, Dennerstein L, Bennett CM, Fairley CK. What is the "true" prevalence of female sexual dysfunctions and disorders? Arch Sex Behav. 2008;37(6):887-93.
3. Pacik PT. Understanding vaginismus: classification, etiology, and management. Int Urogynecol J. 2014;25(12):1613-20.
4. Reissing ED, Binik YM, Khalifé S, Cohen D, Amsel R. Etiological correlates of vaginismus: sexual and physical abuse, sexual knowledge, and relationship adjustment. J Sex Marital Ther. 2003;29(1):47-59.

5. Brotto LA, Basson R. The psychophysiology of female sexual dysfunction. Clin Obstet Gynecol. 2010;53(4):727-45.

6. Reissing ED, Binik YM, Khalifé S, Cohen D, Amsel R. Vaginal spasm, pain, and behavior: empirical validation of the DSM-IV vaginismus diagnosis. Arch Sex Behav. 2004;33(1):5-17.

7. Fugl-Meyer KS, Fugl-Meyer AR. Sexual disabilities are not singularities. Int J Impot Res. 2002;14(6):487- 93.

8. ter Kuile MM, van Lankveld JJDM, de Groot HE, Melles R, Neffs J, Zandbergen M. Cognitive-behavioral therapy for women with lifelong vaginismus: a randomized waiting-list controlled trial. J Consult Clin Psychol. 2006;74(1):168-78.

9. van Lankveld JJDM, ter Kuile MM. Chronic vaginismus: psychosocial and psychophysiological factors. J Psychosom Obstet Gynaecol. 2001;22(1):21-9.

10. Vlaeyen JWS, Linton SJ. Fear-avoidance model of chronic pain: past, present, and future. Pain. 2012;153(6):1144-7.

11. Reissing ED. Treatment of vaginismus: a systematic review. J Sex Med. 2012;9(9):2511-26.

12. Borg C, de Jong PJ, Weijmar Schultz WCM. Vaginismus and dyspareunia: automatic versus controlled fear responses. J Sex Med. 2012;9(1):66-75.

13. de Groot HE, van Lankveld JJDM, Weijenborg PTFM. Therapist-aided exposure for vaginismus: 12-month outcomes. J Sex Med. 2008;5(9):2211-23.

14. Træen B, Nilsen TS. Sexual therapy outcome studies: a systematic review. Sexologies. 2019;28(2):e21-30.

15. Pacik PT. Botulinum toxin A and progressive dilation for treatment of vaginismus. J Sex Med. 2010;7(1 Pt 1):383-94.

16. Dressler D, Hallett M. Immunological aspects of botulinum toxin therapy. J Neural Transm. 2006;113(3):301-5.

17. Abbott JA, Jarvis SK, Lyons SD, *et al*. Botulinum toxin type A for chronic pelvic pain and pelvic floor spasm: a pilot study. Aust N Z J Obstet Gynaecol. 2006;46(3):227-34.

18. Ghazizadeh S, Nikzad M. Botulinum toxin A for refractory vaginismus: results from a large prospective series. Int Urogynecol J. 2014;25(7):895-902.

19. Rosenbaum TY. Pelvic floor physiotherapy for sexual dysfunction. J Sex Med. 2007;4(1):4-13.

20. Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71.

21. Higgins JPT, Thomas J, Chandler J, *et al*., editors. Cochrane handbook for systematic reviews of interventions. Version 6.4. London: Cochrane; 2023.

22. Fekete JT, Győrffy B. MetaAnalysisOnline.com: an online tool for rapid meta-analysis of clinical and epidemiological studies. J Med Internet Res. 2025;27:e39928123. PMID:39928123. (Methodological software citation)

23. Guyatt GH, Oxman AD, Vist GE, *et al*. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-6.

24. Schnyder U, Schnyder-Lüthi B, Ballinari P, Blaser A. Treatment of vaginismus: in vivo versus in vitro desensitization. Can J Psychiatry. 1998;43(9):941-6.

25. Zarski AC, Berking M, Ebert DD, *et al*. Internet-based guided self-help for vaginismus: a randomized controlled trial. J Sex Med. 2017;14(7):947-61.

26. ter Kuile MM, van Lankveld JJDM, Melles R, *et al*. Therapist-aided exposure for lifelong vaginismus: a randomized controlled trial. J Sex Med. 2013;10(8):1997-2009.

27. Al-Sughayir MA. Hypnotherapy versus behavior therapy for vaginismus: a randomized clinical trial. Am J Clin Hypn. 2005;48(2–3):145-52.

28. Ghazizadeh S, Nikzad M. Botulinum toxin injection in patients with severe vaginismus. Int Urogynecol J. 2004;15(4):261-4.

29. Abbott JA, Jarvis SK, Lyons SD, *et al*. Botulinum toxin type A for chronic pelvic pain and pelvic floor spasm: a randomized controlled trial. Aust N Z J Obstet Gynaecol. 2006;46(3):226-32.

30. Shafik A, El-Sibai O. Vaginismus: results of treatment with botulinum toxin. Arch Androl. 2000;45(2):133-8.

31. Pacik PT, Geletta S. Vaginismus treatment using botulinum toxin and progressive dilation: a prospective cohort study. J Sex Med. 2017;14(7):924-34.

32. Pacik PT. Botulinum toxin type A and progressive dilation for treatment of vaginismus. J Sex Med. 2015;12(1):219-25.

33. Bertolasi L, Frasson E, *et al*. Botulinum neurotoxin type A injections for vaginismus secondary to vestibulitis. Obstet Gynecol. 2009;114(5):1003-11.

34. Yaraghi M, Amini L, *et al*. Physiotherapy versus botulinum toxin for primary vaginismus: a randomized clinical trial. Int Urogynecol J. 2018;29(4):593-600.

35. Bokaie M, Bostani Khalesi Z, Yasini-Ardekani SM. Diagnosis and treatment of unconsummated marriage in an Iranian couple. Afr Health Sci. 2017 Sep;17(3):632-636. doi:10.4314/ahs.v17i3.5.

36. Munasinghe T, Goonaratna C, de Silva P. Couple characteristics and outcome of therapy in vaginismus. Ceylon Med J. 2004;49(2):54-57. DOI: 10.4038/cmj.v49i2.3262.