

# Conservative management of Type III A/B chronic prostatitis/chronic pelvic pain syndrome: a systematic review

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## ABSTRACT

**Background** Chronic prostatitis or chronic pelvic pain syndrome (CP/CPPS) is a debilitating condition and diagnosing and managing this condition is challenging.

**Objectives** A systematic review was conducted to: (i) investigate the effects of conservative management on people with Type III A/B CP/CPPS; (ii) review study enrolment criteria used to enrol participants with Type III A/B CP/CPPS; (iii) investigate the description of the diagnostic outcomes and corresponding interventions used across studies.

**Methods** Electronic databases were searched to September 2024. Outcomes assessed included pain, urinary symptoms and quality of life. Included studies were assessed using the Template for Intervention Description and Replication checklist, Joanna Briggs Institute critical appraisal checklist, and the Grading of Recommendation, Assessment, Development, and Evaluations guideline.

**Results and Discussion** Twenty studies were included. GRADE evidence quality was very-low for all studies. Electrical stimulation and non-electrotherapy intervention showed improvements in pain, urinary symptoms and quality of life. Electromagnetic therapy did not improve reported outcomes. Studies reporting adverse events were mild and transient. Enrolment criteria used to diagnose Type III A/B CP/CPPS were varied. Most interventions targeted the pelvic floor only despite patients' reported pain locations and the outcomes of the diagnostic outcomes reported in each study.

**Conclusion** Preliminary findings suggests that electrical stimulation is a promising intervention for pain, urinary symptoms and QoL. Adjunct therapies including pelvic floor biofeedback and targeted manual therapy can be considered, if supported by examination findings. Interventions should be tailored based on patients' clinical presentations and specific exam findings.

**Keywords** male genitourinary disease, genitourinary systems, electrotherapy, conservative management, chronic pelvic pain syndrome

## INTRODUCTION

Chronic prostatitis or chronic pelvic pain syndrome (CP/CPPS) is defined as pain, pressure, or discomfort localised in the pelvic region, perineum, or genitalia that lasts for more than three months, without the presence of uropathogenic bacteria.<sup>1</sup> The prevalence rate of CP/CPPS varies from 2% to 25%.<sup>2,3</sup> This variation is likely explained by various factors including genetics, ethnic groups, cultural backgrounds, educational levels, psychological status, lifestyles, food habits, health status, family relationships, and socioeconomic conditions.<sup>3</sup>

A variety of surgical, non-surgical, and alternative therapies have been suggested for the management of CP/CPPS but the evidence supporting the clinical effectiveness of these interventions is limited.<sup>4</sup> It is important to note that while other classification systems, such as the European Association of Urology Classification of Chronic Pelvic Pain Syndromes, can be used to categorise chronic pelvic pain syndromes into different domains, UPOINT is more specific to men with CP/CPPS.<sup>5</sup> The UPOINT classification categorises CP/CPPS patients into six domains, allowing for holistic healthcare provision: urinary, psychosocial, organ-specific, infection, neurologic, and tenderness

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of skeletal muscles.<sup>6</sup> The model proposes that patients who test positive in any of these domains should be referred to and managed by appropriate healthcare professionals.<sup>7</sup> If skeletal muscle tenderness is present, conservative management via referral to physiotherapy is recommended.<sup>6</sup> While established CP/CPPS guidelines strongly support the use of physiotherapy interventions,<sup>8</sup> the treatments offered have shown varying clinical effectiveness and rely on empirical evidence.<sup>9</sup> This variability may be attributed to the complex nature of the condition and lack of personalised interventions in studies.<sup>10</sup> Thus, the primary aim of this study is to investigate how conservative interventions impact symptoms, physical function, and quality of life (QoL) in individuals with CP/CPPS.

Diagnosing CP/CPPS is challenging due to the lack of robust epidemiological data and the overlap of symptoms with other urological conditions.<sup>7</sup> To improve the diagnostic process, the Prostatitis Expert Reference Group (PERG) in the United Kingdom developed a consensus guideline, recommending tests such as digital rectal examination (DRE), abdominal examination, urine dipstick analysis (UDA), mid-stream urine (MSU) culture and microscopy.<sup>7</sup> If there are suspicions of other urological conditions, prostatic specific antigen (PSA) tests, uroflowmetry, retrograde urethrography or cystoscopy, transrectal ultrasound, prostate biopsy, urethral swabs and culture, magnetic resonance imaging, and screening for sexually transmitted infections (STIs) should be considered.<sup>7</sup> However, it is unclear whether these examinations were routinely performed before the diagnosis of CP/CPPS. Therefore, the secondary aim of this study is to document and review the study enrolment criteria used for diagnosing and enrolling participants with Type III A/B CP/CPPS.

Patients with CP/CPPS experience pain in multiple urogenital areas, such as the perineum, suprapubic region, testicles, penis, rectum, abdomen, groin, inguinal area and lower back.<sup>7</sup> While multiple conservative management approaches were recommended, it is unclear whether the interventions provided by clinicians were specifically tailored to address the pain locations reported by the patients.<sup>4</sup> Furthermore, it is unclear whether the management resulted in improvement at a single or multiple locations, limiting clinicians' ability to understand the relationship between the intervention and patients' pain location. Therefore, the tertiary aim is to investigate the description of the diagnostic outcomes and corresponding interventions utilised in the included studies.

## METHODS

### Protocol and registration

This systematic review protocol was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and has been registered on the PROSPERO database (ID: CRD42022381863).

### Study design and participants

Only full-text articles published in English were considered. Study designs included randomised controlled trials (RCTs), prospective (comparative) cohort studies, case-control studies, and retrospective case series with two or more participants. Eligible studies included men (at least 50% male participants) aged  $\geq 18$  years of age with a clinical diagnosis of a Type III A/B CP/CPPS. To identify all relevant conservative interventions and their effects on symptoms, physical function and quality of life in individuals with CP/CPPS, conditions that share overlapping symptoms with CP/CPPS, such as chronic orchialgia, chronic scrotal pain syndrome, and pudendal neuralgia were also included. Type I, II and IV CP/CPPS were excluded.

### Interventions and comparators

Interventions of interest for this review were confined to physiotherapy-led only. This included various exercise modalities (strengthening, stretching, aerobic, relaxation, and breathing strategies), electrotherapeutic modalities (transcutaneous electrical nerve stimulation [TENS], and therapeutic ultrasound) and manual therapies (dry needling, massage, and manual mobilisation techniques). Comparators that were considered included non-pharmacological or pharmacological interventions, surgical management; wait-and-see approach, and education.

### Outcomes measures

Outcome measures that assess symptoms (pain, urinary) and QoL were included. Intervention duration data was extracted and categorised as short-term ( $\leq 12$  weeks), medium term ( $>12$  weeks to  $\leq 6$  months) and long term ( $>6$  months). Adverse events were reported as secondary outcomes, categorised into minor or major.<sup>11</sup> Minor adverse events were defined as incidents having minimal serious or potentially serious effects, such as short-lasting discomfort or sensory changes.<sup>12</sup> Major adverse events were incidents that had potential for severe effects, such as permanent functional disability.<sup>12</sup>

### Search method and selection of studies

A systematic literature search was conducted up to September 2024 for relevant studies published in MEDLINE, CINAHL, EMBASE, and AMED. A comprehensive search using a combination of keywords and medical subject headings (MeSH) was undertaken with assistance of a librarian (EH). The search strategy was formed around two concepts: "chronic prostatitis/chronic pelvic pain syndrome" and "physiotherapy-led interventions". Synonyms within each concept were combined with the OR Boolean operator; and terms between concepts were combined with the AND Boolean operator (Appendix 1). No language or publication period restrictions were imposed. Manual citation tracking (Google Scholar) and reference checking of included articles, narrative and systematic reviews on the topic were also conducted.

References were imported into Covidence, a systematic review software (Veritas Health Innovation, Melbourne, Australia) for duplicate screening. Two reviewers (RH and RW or DC) independently reviewed the titles and abstracts of the articles for eligibility. Abstracts that did not meet the eligibility criteria were excluded, and any disagreements between the reviewers were resolved with input from a third reviewer (AS). Full text versions of the remaining articles were further screened for eligibility by two independent reviewers (RH and AS).

Pre-specified data, such as the eligibility criteria, study design, participant demographics, intervention, outcome measures, results at all time points and adverse events were extracted by RH and verified by AS. Author(s) of relevant papers were contacted via email when data was missing. If the author(s) did not respond to a second follow-up email two weeks after the initial email, raw data was reported.

### Data collection and analysis

Means and standard deviations (SDs) of continuous outcome measures for comparative studies were converted to standardised mean differences (SMD) with a 95% confidence interval (CI) using RevMan (version 5.4.1). If SDs were not reported, they were imputed where possible using formulas described in the Cochrane handbook (<https://training.cochrane.org/handbook>); or extracted from graphs (<https://automeris.io/WebPlotDigitizer/>). Effective sizes of  $\geq 0.2$ ,  $\geq 0.5$  and  $\geq 0.8$ , were defined as small, medium, and large respectively.<sup>13</sup> Statistical heterogeneity across the pooled studies was evaluated using the I<sup>2</sup> statistic. A low, moderate, or high level of heterogeneity was determined based on an I<sup>2</sup> value of 25%, 50%, or 75%, respectively.<sup>11</sup>

### Quality assessment

The CP/CPPS diagnostic criteria for each study were evaluated using the criteria proposed by the PERG.<sup>7</sup> The methodological quality of the included studies was assessed by two reviewers (RH and AS) using the Joanna Briggs Institute (JBI) critical appraisal checklist for RCTs, quasi-experimental study (non-RCT), and case series.<sup>14</sup> Reviewers scored the items listed on each checklist using: yes (Y); no (N); unclear (U); or not applicable (N/A). Study scores  $\leq 50\%$ , 50-70%, and  $\geq 70\%$  were classified as: low; medium; and high quality, respectively.<sup>15</sup>

Completeness of reporting intervention and control groups was assessed using the Template for Intervention Description and Replication Checklist (TI-DieR).<sup>16</sup> This checklist is to determine if the study of interest has included sufficient information relating to the treatments used to allow replication in research or clinical practice.<sup>16</sup> Items were scored N/A if they were not applicable; or '?' if information about the element was not, or insufficiently, reported.<sup>16</sup>

The Grading of Recommendation, Assessment, Development, and Evaluations (GRADE) guidelines were used to examine the quality of the outcomes of the included studies.<sup>17</sup> The quality of the evidence was

graded as high, moderate, low, or very low depending on the nature of the study.<sup>17</sup> RCTs were considered to be high quality, whereas uncontrolled case series were considered as very low-quality evidence.<sup>17</sup> The quality of each study was either downgraded or upgraded based on the following criteria: (i) risk of bias (downgraded if  $\geq 25\%$  of the participants from studies demonstrated a high risk of bias as per risk of bias tool), (ii) inconsistency (downgraded if there was significant statistical heterogeneity, I<sup>2</sup>  $> 40\%$ ), (iii) indirectness (downgraded if heterogeneous population or intervention), (iv) imprecision (downgraded if total number of participants  $< 300$  for each outcome and wide confidence intervals, and (v) other considerations (downgraded if publication bias, flawed design, and massive dropout were identified).<sup>17</sup> Single studies with a sample size of less than 300 were considered to have limitations in terms of inconsistency and imprecision, leading to a classification of 'low-quality evidence'.<sup>18</sup> If additional items were not satisfied, the quality of evidence could be further downgraded to 'very low-quality evidence'.<sup>17</sup>

## RESULTS

### PRISMA

The PRISMA flow diagram (Figure 1) illustrates the identification process of studies through database searching. A total of 10,781 studies were initially identified, and the full texts of 120 studies were assessed for inclusion. Twenty studies met the predetermined inclusion criteria.

### Demographics

The study design and patient characteristics are displayed in Appendix 2. The total number of recruited participants included in this review was 711. The mean ages across studies ranged from 26 to 69 years. The duration of symptoms in the studies varied from 3 to 300 months.

### TI-DieR

Reporting of included interventions of all studies was assessed using TI-DieR checklist and is reported in Appendix 3. Between 81-100% of the studies described the intervention, including its rationale, frequency, duration, as well as materials and procedures related to the interventions. Contrarily, other items were inadequately described, with a rating of 0-67%.

### Outcome measures

Pain, urinary symptoms, and QoL were commonly evaluated using the National Institute of Health Chronic Prostatitis Symptom Index (NIH-CPSI) questionnaire in most studies ( $n = 14$ ), whereas a handful of studies measured pain and urinary symptoms using visual analogue scale (VAS) or numerical rating scale (NRS) ( $n = 5$ ) (Table 1). One case study used narrative to describe its outcome. The follow-up times ranged from 4 weeks to 382 weeks.

Table 1. Study results

Study (Year)	Intervention	Mean follow up (range)	Pain Mean/median before and after treatment (p value), where applicable	Urinary symptoms Mean/median before and after treatment (p value), where applicable	Quality of life Mean/median before and after treatment (p-value), where applicable	Adverse event (number %): minor, major
<b>RCTs</b>						
Kabay et al (2009) <sup>19</sup>	<b>PTNS vs Sham PTNS</b> <b>PTNS</b> 30 minutes, pulse rate of 20Hz, intensity (1-10mA), 12 sessions <b>Sham PTNS</b> 30 minutes, electrical stimulation not applied	12 weeks	NIH-CPSI -1.97 SMD [95% CI -2.48, -1.46] -ve favours experimental (PTNS)	NIH-CPSI -2.32 SMD [95% CI -2.86, -1.77] -ve favours experimental (PTNS)	NIH-CPSI -2.83 SMD [95% CI -3.43, -2.24] -ve favours experimental (PTNS)	NR
Kessler et al (2014) <sup>18</sup>	<b>EMT vs sham EMT</b> <b>EMT</b> Twice 10 minutes daily; ultrasound intensity of 100 mW/cm <sup>2</sup> with an ultrasonic power of 12 mW and a frequency of 1.9 MHz; electric field force of 3 V/m and magnetic field force of 0.4 A/m <b>Sham EMT</b> No stimulation applied	6 weeks, 12 weeks, 16 weeks	NIH-CPSI 12 weeks: -0.31 SMD [95% CI -0.82, 0.20] 16 weeks: -0.21 SMD [95% CI -0.72, 0.30] -ve favours experimental (EMT)	NIH-CPSI 12 weeks: 0.00 SMD [95% CI -0.51, 0.51] 16 weeks: 0.07 SMD [95% CI -0.44, 0.58] +ve favours control (Sham EMT)	NIH-CPSI 12 weeks: -0.51 SMD [95% CI -1.03, 0.00] 16 weeks: -0.51 SMD [95% CI -1.03, 0.01] -ve favours experimental (Sham EMT)	0%
Paick et al (2006) <sup>21</sup>	<b>EMT + medication vs medication</b> <b>EMT + medication</b> 20 minutes, twice a week for 6 weeks, frequency of the pulse field was 10Hz; intermittently for 10 minutes, followed by a rest period of 2 minutes; and a second treatment at 50Hz intermittently for 10 minutes. 2 mg alpha-blockers once per day for the first 7 days, and increase to receive 4 mg once daily for the following 5 weeks <b>Medication</b> Same prescription dosages and frequency as above	6 weeks	NIH-CPSI -0.20 SMD [95% CI -0.83, 0.42] -ve favours experimental (EMT + medication)	NIH-CPSI 0.07 SMD [95% CI -0.55, 0.69] +ve favours control (medication)	NIH-CPSI 0.23 SMD [95% CI -0.39, 0.86] +ve favours control (medication)	0%

Study (year)	Intervention	Mean follow up (range)	Pain Mean/median before and after treatment (p value), where applicable	Urinary symptoms Mean/median before and after treatment (p value), where applicable	Quality of life Mean/median before and after treatment (p-value), where applicable	Adverse event (number %): minor, major
Pandey et al (2020) <sup>23</sup>	<b>ES + biofeedback vs multi-modal therapies</b> <b>ES + biofeedback</b> 2 sessions per week for 4 weeks, then 1 session per week for 8 weeks, thus completing a total of 12 weeks of therapy. Regular contraction and relaxation exercises regularly at home <b>Multi-modal therapies</b> Alpha blockers, anti-inflammatory agents, sitz bath for 3 months	12 weeks, 24 weeks	NIH-CPSI 12 weeks: -0.04 SMD [95% CI -0.48, 0.40] 24 weeks: -0.46 SMD [95% CI -0.90, -0.01] -ve favours experimental (ES + biofeedback)	NIH-CPSI 12 weeks: -0.01 SMD [95% CI -0.45, 0.43] 24 weeks: -0.46 SMD [95% CI -0.91, -0.01] -ve favours experimental (ES + biofeedback)	NIH-CPSI 12 weeks: -0.01 SMD [95% CI -0.45, 0.43] 24 weeks: -0.46 SMD [95% CI -0.90, -0.01] -ve favours experimental (ES + biofeedback)	0%
Rowe et al (2005) <sup>24</sup>	<b>EMT vs Sham EMT</b> <b>EMT</b> 2 sessions weekly for 4 weeks. 30 minutes each session, 2 consecutive 15-minute periods, 10 Hz for the first 15-minute period and increased to 50 Hz for the second 15-minute period <b>Sham EMT</b> Same prescription as active group except no active stimulation was applied from the device.	4 weeks, 52 weeks	VAS 4 weeks: -0.95 SMD [95% CI -1.98, 0.08] 52 weeks: -1.23 SMD [95% CI -2.48, 0.03] -ve favours experimental (EMT)	VAS 4 weeks: -1.03 SMD [95% CI -2.07, 0.02] 52 weeks: -0.56 SMD [95% CI -1.70, 0.59] -ve favours experimental (EMT)	NR	Mild - EMT: 1/10 (10%) - Sham EMT: 0/10 (0%)
Samhan et al (2011) <sup>22</sup>	<b>TENS + Abx + Analgesics vs Sham TENS + Abx + Analgesic</b> <b>TENS + Abx + Analgesia</b> 5 times per week for 4 consecutive weeks, daily 20 minutes, mean frequency (100Hz), mean pulse width (100µs) and mean intensity (25mA) <b>Sham TENS + Abx + Analgesia</b> 5 times per week for 4 consecutive weeks, 20 minutes daily	4 weeks	NIH-CPSI -3.76 SMD [95% CI -4.83, -2.69] -ve favours experimental (TENS + Abx + Analgesics)	NR	NR	NR

Study (year)	Intervention	Mean follow up (range)	Pain Mean/median before and after treatment (p value), where applicable	Urinary symptoms Mean/median before and after treatment (p value), where applicable	Quality of life Mean/median before and after treatment (p-value), where applicable	Adverse event (number %): minor, major
Lamina et al (2008) <sup>20</sup>	<b>TENS + Abx vs Sham tablets + Abx</b> <b>TENS + Abx</b> 20 minutes, mean frequency, pulse width and intensity of 100Hz, 100µs and 25mA respectively, daily, 5 times per week for 4 consecutive weeks (average of 20 treatment sessions); and ofloxacin (300 mg) thrice daily <b>Sham tablets + Abx</b> Placebo tablet twice daily; and ofloxacin 300 mg thrice daily	17 weeks	NIH-CPSI pain -5.09 SMD [95% CI -7.34, -2.83] -ve favours experimental (TENS + Abx)	NR	NR	NR
Sevim et al (2023) <sup>20</sup>	<b>TTNS vs PTNS</b> <b>TTNS</b> 30 minutes, once a week for 12 weeks, 20Hz, 200µs, 10mA-20mA <b>PTNS</b> 30 minutes, once a week for 12 weeks, 20HBz, 200µs, 5-10mA	12 weeks	1.22 SMD [95% 0.47, 1.97] +ve favours control (PTNS)	0.23 SMD [95% -0.11, 0.57] + favours control (PTNS)	0.45 SMD [95% 0.07, 0.83] + favours control (PTNS)	0%
Tantawy et al (2017) <sup>25</sup>	<b>TENS + Analgesia</b> 5 times per week for 4 weeks (TENS frequency, 100 Hz; pulse width, 100µs; duration, 30 minutes), intensity (mean 25mA) <b>Analgesia</b> Not described	12 weeks	VAS -2.20 SMD [95% CI -2.84, -1.57] -ve favours experimental (TENS + Analgesia)	NR	NR	NR
<b>Non-RCT</b>						
Yang et al (2017) <sup>26</sup>	<b>EMT</b> 30 minutes, twice weekly, for 6 weeks. Frequency 10Hz for 15 minutes, followed by 70 Hz for 15 minutes <b>ESB (ES + biofeedback)</b> ES twice weekly for 2 weeks, followed by once a week for 4 weeks. Each session lasted about 45 minutes and included 15 minutes of biofeedback, followed by 30 minutes of ES. The frequency prescribed was the same as EMT Pelvic floor biofeedback consists of detailed instructions on how to contract and relax the pelvic floor muscles under the guidance of palpation of the pelvic floor muscles and biofeedback measurements	18 weeks	NIH-CPSI Pain 2.30 SMD [95% CI 0.20, 4.40] +ve favours experimental (EMT)	NIH-CPSI Urinary 0.10 SMD [95% CI 1.12, -1.3] +ve favours experimental (EMT)	NIH-CPSI QOL 2.10 SMD [95% CI 4.13, -0.13] +ve favours experimental (EMT)	0%

Study (year)	Intervention	Mean follow up (range)	Pain Mean/median before and after treatment (p value), where applicable	Urinary symptoms Mean/median before and after treatment (p value), where applicable	Quality of life Mean/median before and after treatment (p-value), where applicable	Adverse event (number %): minor, major
<b>Case Series</b>						
Ajimsha et al (2021) <sup>27</sup>	<b>EMM Therapy</b> Treated areas include: (1) right EO, left IO and HAC; (2) left EO, right IO and HAC; (3) right LD, TLF and left GMx; (4) left LD, TLF and right GMx; (5) EMM of the abdomino-pelvic viscera 5 sessions once a week, each session having an average duration of 30 min	6 weeks	NIH-CPSI Pain Mean difference (SD), 95% CI 13.44 (3.12) (95% CI 12.42, 13.94), p<0.001	NIH-CPSI Urinary Mean difference (SD), 95% CI 2.97 (1.83) (95% CI 2.42, 3.64), p<0.001	NIH-CPSI QoL Mean difference (SD), 95% CI 3.74 (2.15) (95% CI (3.17/4.30), p<0.001	For session 1: 36% (pain), 16% (dysuria), 10% (feverish), 26% (skin discoloration). For session 2, these symptoms reduced to 19% (pain), 7% (dysuria), 3% (feverishness), 26% (discoloration). For session 3, they reduced further to 10% (pain), 0% (dysuria, feverishness), 7% skin discoloration. No symptoms reported by session 4 and 5.
Chouhan et al (2020) <sup>28</sup>	<b>Physical therapy</b> (treatments provided NR)	12 weeks	"complete resolution"	NR	NR	NR
Clemens et al (2000) <sup>29</sup>	<b>Pelvic floor biofeedback and bladder retraining</b> 6 biweekly visits, each lasting 1 hour	5.8 months (range 1.6 to 14.8)	VAS [pain] Median 5 (0-8) to 1 (0-3), p=0.001	AUA urinary symptom scores Median 15 (0-26) to 7.5 (0-19), p=0.001	NR	NR
Cornel et al (2005) <sup>30</sup>	<b>Pelvic floor biofeedback and exercises</b> Initially once a week, followed by once every 2-4 weeks	15-29 weeks	NIH-CPSI Pain Mean 11 (range 2-16) to 5.7 (range 1-13), p<0.001	NIH-CPSI Urinary Mean 5.1 (range 0-10) to 2.2 mean (range 0-6), p<0.001	NIH-CPSI QoL Mean 7.3 (range 2-11) to 3.5 (range 0-10), p<0.001	NR
Farrell et al (2016) <sup>31</sup>	<b>Multi-modal therapies</b> Pelvic floor biofeedback and home exercise program, medical management of constipation. Details of treatment NR	median 13 months follow-up (range 3-48 months)	NRS Pain Median 6/10 (range 2-10) to 4.5/10 (range 1-10)	NR	NR	NR
He et al (2010) <sup>34</sup>	<b>Pelvic floor biofeedback</b> ≈30 min, 2 or 3 times a week, and could be done intermittently for several weeks	10 weeks	NIH-CPSI PAIN Mean (SD) 4.0 ± 2.0 to 2.2 ± 1.7, p<0.001	NIH-CPSI URINARY Mean (SD) 7.9 ± 2.1 to 2.2 ± 1.9, p<0.001	NIH-CPSI QoL Mean (SD) 9.6 ± 2.7 to 2.9 ± 2.6, p<0.001	NR

Study (year)	Intervention	Mean follow up (range)	Pain Mean/median before and after treatment (p value), where applicable	Urinary symptoms Mean/median before and after treatment (p value), where applicable	Quality of life Mean/median before and after treatment (p-value), where applicable	Adverse event (number %): minor, major
Khandwala et al (2017) <sup>35</sup>	<b>External vibratory stimulation</b> Applied at the location of external ring for 20 minutes per day for 4 weeks	4 weeks	VAS Pain Mean 4.9 to 2.7 (p=0.009) Maximum pain severity Mean 6.3 to 4.0 (p=0.013)	NR	NR	Mild 3 /9 (33%)
Masterson et al (2017) <sup>36</sup>	<b>Multi-modal therapies</b> (I) manual therapy for myofascial trigger point release (internal and external manipulation of the pelvic floor and abdominal musculature) (II) therapeutic exercises (i.e. range of motion, mobility, flexibility and strengthening exercises) (III) pelvic floor biofeedback (IV) neuromodulation for pain relief	44-192 weeks	NIH-CPSI Total 30.8 (16 to 39) to 22.2 (7 to 37)	NR	NR	NR
Conesa et al (2022) <sup>32</sup>	<b>Multi-modal therapies</b> Muscular and ligamentary manual therapy, articular manual therapy, vascular and neurovegetative system therapy	10 weeks, 16 weeks, 22 weeks	NIH_CPSI PAIN Mean difference 2.49 [95% CI -0.09, 4.18]	NIH_CPSI Urinary Mean difference 1.16 [95% CI 0.05, 2.33]	NIH_CPSI QOL Mean difference 1.98 [95% CI 0.51, 3.02]	0%
Schneider et al (2013) <sup>33</sup>	<b>TENS</b> 80Hz and 150ms at the sensory threshold level for 30 minutes, twice a day	12 weeks, 43.6 months (range 6-88 months) follow-up mean (95% CI; range) follow-up of 43.6(33.2-56; 6-88) months in 21 (72%) of 29 patients	Mean 6.6 (95% 6.3, 6.9) to 3.9 (95%CI 3.2, 4.6), p<0.001	NR	NR	0%



Study (year)	Intervention	Mean follow up (range)	Pain Mean/median before and after treatment (p value), where applicable	Urinary symptoms Mean/median before and after treatment (p value), where applicable	Quality of life Mean/median before and after treatment (p-value), where applicable	Adverse event (number %): minor, major
<sup>a</sup> Van Alstyne et al (2010) <sup>37</sup>	<b>Multi-modal therapies</b> Individualised therapies including abdominal and transrectal trigger point release; pelvic floor relaxation, aerobic, stretching, postural strengthening exercises; moist heat	11 visits 7 visits follow-up 1 year	NIH-CPSI Pain <u>Patient 1</u> 14 to 0 <u>Patient 2</u> 16 to 12 NPRS (post PT visits) <u>Patient 1</u> 9 to 0 <u>Patient 2</u> 8 to 4 NPRS (1 year) 0 for both patients	NIH-CPSI Urinary <u>Patient 1</u> 1 to 0 <u>Patient 2</u> 4 to 2	NIH-CPSI QoL <u>Patient 1</u> 10 to 0 <u>Patient 2</u> 9 to 7	NR

Abbreviations: Antibiotics (Abx); American Urological Association (AUA), confidence interval (CI), external myofascial mobilization (EMM), electromagnetic therapy (EMT), electrical stimulation (ES), ipsilateral latissimus dorsi (LD); ipsilateral thoracolumbar fascia (TLF) and contralateral gluteus maximus (GMx) posteriorly; and ipsilateral external oblique (EO) and contralateral internal oblique (IO); and hip adductor complex (HAC) anteriorly; National Institute of Health Chronic Prostatitis Symptom Index (NIH-CPSI) peripheral tibial nerve stimulation (PTNS), NR (not reported), numerical rating scale (NRS), randomized controlled trial (RCT), standard deviation (SD), standardized mean difference (SMD), transcutaneous electrical nerve stimulation (TENS), visual analogue scale (VAS)

<sup>a</sup> = Follow-up duration in weeks was unclear. Data reported in number of physical therapy visits.

**Risk of bias**

The risk of bias for RCTs, non-RCT and case series are presented in Appendix 4, Appendix 5 and Appendix 6, respectively. Among the RCTs, there were two high quality studies,<sup>20, 21</sup> four medium quality studies,<sup>22-25</sup> and three low quality studies (Appendix 4)<sup>26-28</sup>. The single non-RCT study was high quality (Appendix 5).<sup>29</sup> Out of the 11 case series, seven were high quality<sup>30-36</sup>; one was medium quality<sup>37</sup>; and three were low quality (Appendix 6).<sup>38-40</sup>

**CP/CPPS study enrolment and diagnostic criteria**

Categorising the anatomical locations where the pain was reported by the patients using the NIH-CPSI was not possible as the studies did not provide disaggregated pain locations. However, sufficient information was extracted from the included studies (Appendix 7). The number of pain locations reported varies per study, ranging from one to six, demonstrating the variation in recruitment and enrolment criteria. Amongst these, patients reported pain in the perineum or pelvic floor (PF) in seven studies. However, only one of these seven studies performed PF examinations for perineal pain.<sup>30</sup> In cases where pain was reported in the lower back, hip, groin or pelvis, no studies performed relevant physical examinations for these regions.

The PERG provided a list of recommended assessments for the diagnosis of Type III A/B CP/CPPS.<sup>7</sup> Nine of the 20 studies assessed pain, and three assessed urinary symptoms. However, no studies assessed psychological and sexual dysfunction symptoms (Appendix 8).

Out of the five key recommended assessments by PERG (Appendix 8), only three out of the 21 studies (14%) completed DRE; and none completed abdominal examinations. Twelve studies completed UDA or MSU culture for infectious diseases (57%). Only four studies (19%) completed a PSA test; and no study completed a nucleic acid amplification test to rule out prostate cancer and STIs respectively. To confirm the diagnosis of Type III CP/CPPS, some studies conducted additional tests that were not part of the recommended list, including scrotal ultrasound sonography, post-void residual, semen culture, medication prescription, expressed prostatic secretions, assessment tool and questionnaire administration (Appendix 8).<sup>7</sup>

**Evidence from RCTs**

Very low evidence was found across all studies using the GRADE tool (Appendix 9). It indicates that the data quality is poor and strong recommendations for any interventions cannot be drawn from this review.

**Electrical stimulation (ES)**

A meta-analysis (Figure 2A) reported a large effect [2.80 SMD; 95% 1.05, 4.55] on pain favouring ES compared to sham ES in the short term (≤12 weeks).<sup>22, 25</sup> This is similar to a single RCT that compares ES to analgesia (Figure 2C) [3.32 SMD; 95% 1.67, 4.97]<sup>23</sup>; ES to sham tablets (Figure 2D) [5.09 SMD; 2.83, 7.34]; as well as ES and analgesia to analgesia (Figure 2E) [2.20 SMD; 1.57, 2.84].<sup>28</sup> Contrarily, another study reported no effect [0.04 SMD; 95% 0.40, -0.48] on pain in the short term (≤12 weeks); but small effect [0.46 SMD; 95% 0.01, 0.90] in the long term (>6 months) when comparing

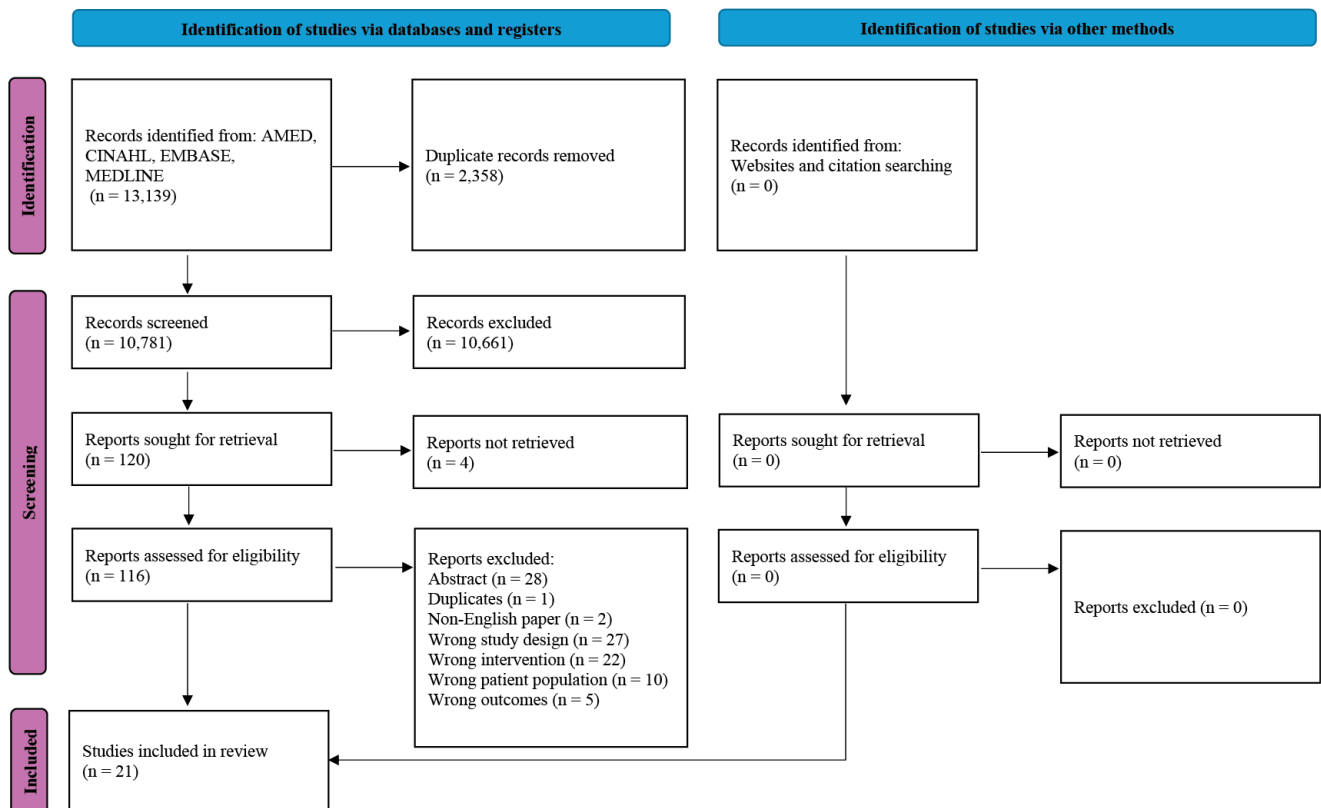


Figure 1. PRISMA flow diagram<sup>19</sup>.

ES and biofeedback to multi-modal therapies (Figure 2G).<sup>26</sup> A study comparing two different types of ES, namely transcutaneous tibial nerve stimulation (TTNS) and peripheral tibial nerve stimulation (PTNS) (Figure 2F), reported large effect [1.22 SMD; 95% 0.47, 1.97] on pain favouring PTNS instead of TTNS in the short term ( $\leq 12$  weeks).<sup>21</sup>

As for urinary symptoms (Figure 3) and QoL (Figure 4), a single study reported a large effect on urinary symptoms (Figure 3B) [2.32 SMD; 95% 1.77, 2.86] and QoL [2.83 SMD; 95% 2.24, 3.43] in the short term ( $\leq 12$  weeks), favouring ES over sham ES.<sup>22</sup> Conversely, another study reported no effect [urinary symptoms (Figure 3D): 0.01 SMD; 95% 0.43, -0.45; QoL (Figure 4C): 0.01 SMD; 95% 0.43, -0.45] in the short term ( $\leq 12$  weeks); but small effect [urinary symptoms (Figure 3D): 0.46 SMD; 95% 0.01, 0.91; QoL (Figure 4C): 0.46 SMD; 95% 0.01, 0.90] in the long term ( $> 6$  months), favouring ES and biofeedback over multi-modal therapies.<sup>26</sup> Another study reported no effect for urinary symptoms (Figure 3C): [0.23 SMD; 95% -0.11, 0.57], however a small effect for QoL (Figure 4B) [0.45 SMD; 95% 0.07, 0.83], favouring PTNS over TTNS in the short term ( $\leq 12$  weeks).<sup>21</sup>

### Electromagnetic therapy (EMT)

A meta-analysis reported no significant effect of improvement in pain [0.47 SMD; 95% -0.07, 1.00] and urinary symptoms (Figure 2B) [0.41 SMD; 95% -0.58, 1.39] in the short term ( $\leq 12$  weeks) when comparing EMT to sham EMT.<sup>20, 27</sup> There was also no significant effect [0.21 SMD, -0.30, 0.72] in the medium term ( $> 12$  weeks to  $\leq 6$  months)<sup>20</sup> and long term ( $> 6$  months) [1.23 SMD; -0.03 to 2.48].<sup>27</sup> For urinary symptoms, it also showed no evidence to indicate a benefit of EMT over sham EMT in the short ( $\leq 12$  weeks), medium ( $> 12$  weeks to  $\leq 6$  months) and long term ( $> 6$  months) (Figure 3A). For the QoL domain, there was a medium effect improvement for the use of EMT compared to sham EMT in both short ( $\leq 12$  weeks) [0.51 SMD; 95% 0.00, 1.03] (Figure 4D) and medium term ( $> 12$  weeks to  $\leq 6$  months) [0.51 SMD; 95% -0.01, 1.03].<sup>20</sup> However, the potential benefit of EMT over sham EMT cannot be confidently ascertained.

When comparing EMT and medication to medication only, there was also no evidence seen in pain (Figure 2H), urinary symptoms (Figure 3E) and QoL (Figure 4E) in the short term ( $\leq 12$  weeks).<sup>24</sup>

### Evidence from non-RCT

A very-low evidence non-RCT<sup>29</sup> that compares EMT to ES and found a large effect improvement in both pain [2.30 SMD; 95% 0.20, 4.40] and possibly QoL [2.10 SMD; 95% 4.13, -0.13] in the medium term ( $> 12$  weeks to  $\leq 6$  months); whereas no improvement in urinary symptom was observed at this timepoint [0.10 SMD; 95% 1.12, -1.32].

### Evidence from case series

There was limited evidence across all case series and the effect sizes were not estimable (Appendix 9).

Outcomes from single case studies are reported in Table 1.

Overall, there was evidence of an improvement in pain in the short-term ( $\leq 12$  weeks) following external myofascial mobilisation (EMM)<sup>30</sup>; TENS<sup>36</sup>; external vibratory stimulation<sup>38</sup>; pelvic floor biofeedback (PFB)<sup>37</sup>; and unspecified physiotherapy intervention.<sup>31</sup> Urinary symptoms and QoL also improved in the following EMM<sup>30</sup> and PFB.<sup>37</sup>

In the medium-term ( $> 12$  weeks to  $\leq 6$  months), improvements in pain and urinary symptoms were observed following PFB and bladder retraining<sup>32</sup>; PFB and exercises<sup>33</sup>; and multi-modal interventions.<sup>34</sup> Similar improvements were noted for QoL following PFB and exercises<sup>33</sup> and multi-modal interventions.<sup>34, 35, 39</sup>

In the long-term ( $> 6$  months), all domains were improved following multi-modal interventions.<sup>39, 40</sup>

### Adverse events

In this review, 33% ( $n=7/21$ ) of the studies assessed showed no adverse events; 14% ( $n=3/21$ ) reported mild adverse events (transient paraesthesia, pain, dysuria, feverishness, skin discoloration); whereas 52% ( $n=11/21$ ) did not report on assessing adverse events (Appendix 10).

## DISCUSSION

The primary aims were to (i) investigate the effects of conservative management on the symptoms, physical function and QoL in people with Type III A/B CP/CPPS; (ii) document and review the study enrolment criteria used to diagnose and enrol participants with Type III A/B CP/CPPS; and (iii) investigate the description of the diagnostic outcomes and the corresponding interventions used across included studies.

Five main findings emerged from the systematic review. There are: (ia) ES is superior when used in isolation or combination with other interventions in improving pain, urinary symptoms and QoL; (ib) EMT did not offer improvements in pain, urinary symptoms and QoL; (ic) non-electrotherapy interventions offered improvements in pain, urinary symptoms and/or QoL when used in isolation or in combination with other therapies; (ii) varied study enrolment criteria were used to diagnose and enrol participants with Type III A/B CP/CPPS; (iii) most interventions targeted the PF only, despite patients' reported pain locations and the outcomes of the diagnostic outcomes reported in each study.

The application and benefits of ES for managing pain have been documented in females experiencing chronic pelvic pain.<sup>41</sup> However, it has been primarily used in females with conditions such as dysmenorrhea, endometriosis, and dyspareunia.<sup>41</sup> This review shows that ES is superior to sham ES<sup>22, 25</sup>; analgesia, sham tablets<sup>23</sup>; and multi-modal therapies<sup>26</sup> in providing a large, clinically meaningful pain relief in the short term ( $\leq 12$  weeks). When ES is combined with analgesic

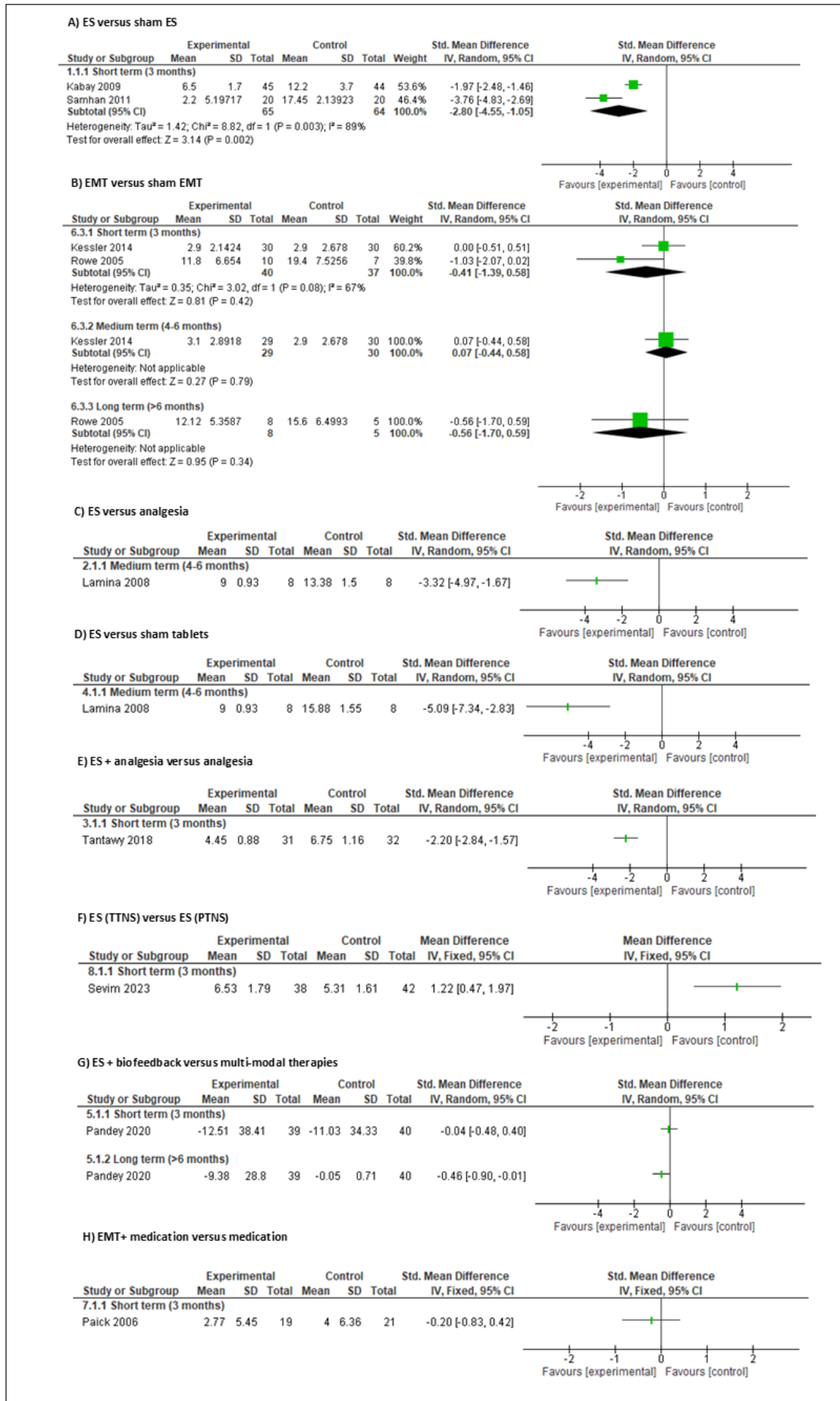


Figure 2. Forest plots - pain

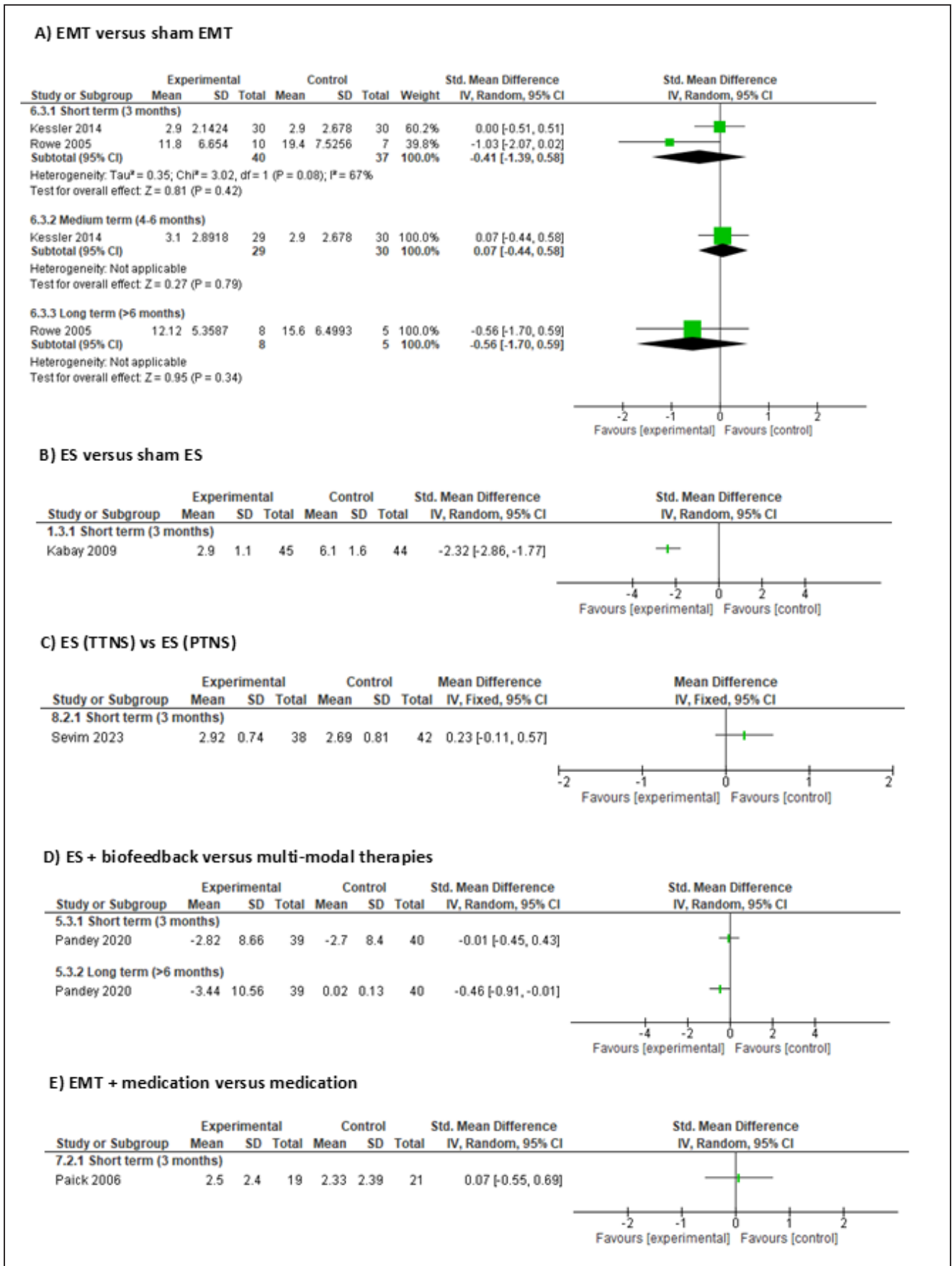


Figure 3. Forest plots - urinary symptoms

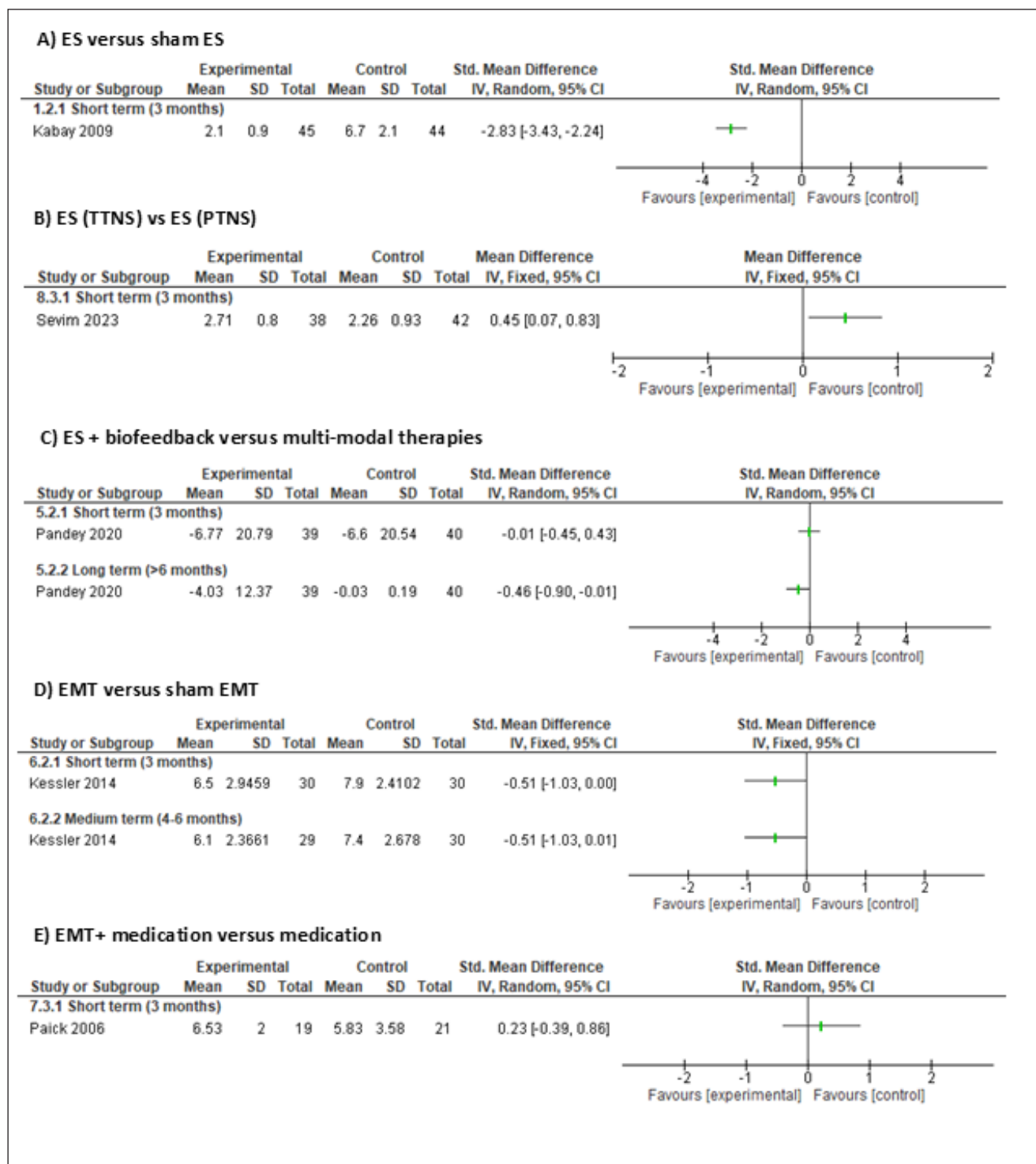


Figure 4. Forest plots - QoL

medications, a similar benefit is seen.<sup>25</sup> There were also preliminary results indicating the benefits of ES in improving urinary symptoms and QoL in the short ( $\leq 12$  weeks) and long term ( $> 6$  months) respectively.<sup>22,26</sup> However, further studies are required before supporting its widespread clinical use on men with CP/CPPS.

It was hypothesised that EMT could improve symptoms by altering the motor and sensory components of the PF, such as PF tonic muscle spasm and neural

hypersensitivity.<sup>42</sup> In this review, EMT did not show clinical and statistical benefits in improving pain, urinary symptoms and/or QoL when compared to sham EMT<sup>27</sup>; and medication<sup>24</sup> in the short ( $\leq 12$  weeks), medium ( $> 12$  weeks to  $\leq 6$  months) and/or long term ( $> 6$  months). While EMT appears to be a safe treatment option, its effectiveness needs to be assessed with larger, more robust clinical trials.

There was a reduction in pain, urinary symptoms and

QoL with manual therapies.<sup>35, 40</sup> These findings are consistent with other studies that have also reported pain improvement following connective tissue manipulation and PF myofascial trigger point release (MTPr),<sup>43</sup> MTPr and paradoxical relaxation training.<sup>44</sup> The changes in patients' symptoms may be attributed to transient pain inhibitory effects on the peripheral and central nervous system; changes to tissue texture, inflammatory biomarkers, behavioural responses such as kinesiophobia; natural recovery; or the placebo effect.<sup>45</sup>

PFB was another intervention that yielded improvement in pain, urinary symptoms and QoL.<sup>32-34, 37, 39</sup> It aims to provide visual feedback of proprioceptive function, to retrain function when PF muscle contraction (PFMC) and relaxation execution is an issue.<sup>46</sup> However, not all studies included in this review had explicitly stated how PFB was delivered, particularly whether PFMC, PF muscle relaxation or a combination of the two were used; and whether verbal instructions were provided along with electromyography or in isolation, and vice versa. Future studies should ensure PFB processes and rationales are included in their methodologies to enable better replication of study interventions. It is important to note that some of the studies in this review included PFMC as part of its relaxation training.<sup>26, 32</sup> It was unclear whether patients were instructed to perform gentle contractions to aid PF muscle relaxation or full muscular contractions. The latter is contrary to the recommendation made by the American Urological Association [AUA] (Grade A evidence) that hypothesises PFMCs may increase pain.<sup>47</sup> However, it is also important to note that 67% (4/6) of the articles cited in the AUA guidelines used PFMC as part of the intervention.<sup>47</sup> These articles reported improved outcomes in NIH-CPSI, AUA symptom and/or VAS scores for women<sup>43, 48</sup> and men.<sup>33</sup> Future studies should provide explicit instructions on the degree of PFMC patients are asked to perform as part of their PF relaxation training.

Vibratory stimulation has been used in other non-urological conditions, such as chronic local or widespread musculoskeletal pain and fibromyalgia.<sup>49</sup> The "gate control theory" stipulates that activating other nerve fibres that conduct non-noxious stimuli, such as vibration can inhibit the peripheral and central nociceptors, thereby reducing an individual's pain severity.<sup>50</sup> While the external vibratory stimulation in this review showed an improvement in pain outcomes, the study had a high risk of bias. Therefore, further studies are required to establish its credibility before recommending it for men with Type III CP/CPPS.

The study enrolment and diagnostic criteria for patients with Type III A/B CP/CPPS were inconsistent across the included studies despite PERG's recommendations for comprehensive subjective, physical and diagnostic assessments.<sup>7</sup> These discrepancies may be attributed to two factors. First, the training of urologists may differ between institutions; and second, in clinical contexts, the thoroughness of subjective and objective examinations may be limited by external time pressure.<sup>51</sup>

Psychological distress and erectile dysfunction are commonly reported by men with CP/CPPS.<sup>52</sup> In this review, no studies have conducted psychological and sexual assessments on men with CP/CPPS. The lack of attention to these symptoms might have contributed to the chronicity (persistence and/or recurrence) of symptoms seen in these men.<sup>53</sup> Furthermore, the pain type experienced by the patients, whether acute, subacute, or chronic, was not assessed and managed accordingly. This may explain the partial resolution of the symptoms experienced by some patients but not others. Future studies should consider incorporating these assessments and evaluating the impact of their management plans on pain, urinary symptoms and QoL.

Musculoskeletal tenderness within the PF is one of the key features of Type III A/B CP/CPPS.<sup>6</sup> However, the UPOINT domain of tenderness (T), which indicates referral to pelvic health physiotherapy, lacks clarity. The description includes tenderness and spasm, which require two separate measures representing pain and tone respectively. This lack of clarity can lead to the mistaken belief that pain and tone are synonymous. Clarifying this domain would aid clinicians in choosing the optimal treatments based on specific patient findings. Furthermore, PF examination is not routinely offered by a urologist, unlike a DRE, which is routinely used to assist the diagnosis of prostate malignancy.<sup>54</sup> This examination differs significantly from the comprehensive PF examination conducted by a specialty-trained pelvic health physical therapist,<sup>54</sup> suggesting that future studies should consider having both medical specialists and physical therapists conduct comprehensive examinations before arriving at a diagnosis of CP/CPPS.

Although multiple pain locations were reported across the included studies, most interventions only targeted the PF without providing a strong rationale for the connection between PF and pain location. While it is plausible that targeting the PF muscles addresses pain experienced in the perineum, peri-anal, anal, rectal, scrotal and testicles, other urological conditions such as bladder, prostate and abdomen could also contribute to pain in these regions. Furthermore, while there were reports of pain improvement, the specific locations where these improvements occurred were not explicitly stated. These findings suggest that clinicians should consider confirming the presence and location of pain reported by the patients as part of their physical assessment and provide a strong rationale for the mechanism of such PF treatment for the clinical presentation.

## Limitations

One of the limitations of this review is the lack of robust clinical trials. The GRADE evidence presented for all interventions appears very low. As a result, making strong recommendations for the use of ES and EMT; or any other interventions on men with CP/CPPS is not possible. Second, pooling of data from other studies was challenging due to considerable heterogeneity

found in the symptoms reported, study designs and interventions provided. Future studies should consider these factors so that the study outcomes are rigorous, replicable, and generalisable to this specific patient cohort.

## CONCLUSIONS

Preliminary findings suggest that ES appears to be a promising intervention for pain, urinary symptoms and QoL when used in isolation or in combination with other therapies. Other forms of intervention such as PFB and targeted manual therapy can be considered as a complementary treatment, if supported by subjective and physical examination findings and strong rationale. At present, there is very low-level evidence supporting the use of any interventions found in this review on men with CP/CPPS. Clinicians should consider individualising treatments based on patients' clinical presentations and specific exam findings until results from high-quality studies with rigorous enrolment criteria and robust RCTs become available.

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## AUTHOR CONTRIBUTION

Conceptualisation: RH. Methodology: RH, AS.

Validation: RH, AS. Formal analysis: RH, AS.

Investigation: RH. Data curation: RH.

Writing, original draft preparation: RH, AS, RW, DC.

Writing, review and editing: RH, AS, RW, DC.

Visualisation: RH, AS. Supervision: RH.

Project administration: RH.

## DATA AVAILABILITY

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## Supplementary material

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