Management of chronic primary pelvic pain syndromes

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Management of chronic pelvic pain (CPP) remains a huge challenge for care providers and a major burden for healthcare systems. Treating chronic pain that has no obvious cause warrants an understanding of the difficulties in managing these conditions. Chronic pain has recently been accepted as a disease in its own right by the World Health Organization, with chronic pain without obvious cause being classified as chronic primary pain. Despite innumerable treatments that have been proposed and tried to date for CPP, unimodal therapeutic options are mostly unsuccessful, especially in unselected individuals. In contrast, individualised multimodal management of CPP seems the most promising approach and may lead to an acceptable situation for a large proportion of patients. In the present review, the interdisciplinary and interprofessional European Association of Urology Chronic Pelvic Pain Guideline Group gives a contemporary overview of the most important concepts to successfully diagnose and treat this challenging disease.

Keywords
pain, chronic primary pain, chronic secondary pain, chronic pelvic pain, chronic primary pelvic pain syndrome, phenotyping, primary bladder pain syndrome, primary prostate pain syndrome, primary scrotal pain syndrome, chronic post-surgical pain

Introduction
Chronic pain syndromes are highly prevalent with a significant negative impact on the quality of life (QoL) of affected individuals [1]. The present article provides an overview of the aetiology, classification, diagnosis, and management of patients with chronic pelvic pain (CPP) syndromes for urologists and other specialists caring for such patients. The evidence underpinning this review has been gathered through systematic literature searches performed by the European Association of Urology (EAU) Chronic Pelvic Pain Guideline Group with regular updates to incorporate the latest available evidence into clinical practice [2]. For more detailed information, the 2021 EAU Guidelines on Chronic Pelvic Pain is available in print and online [2].

Definitions and Terminology
Pain is defined as an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage (International Association for the Study of Pain) [3]. Chronic pain refers to pain lasting for ≥3 months. Now included in the 11th revision of the WHO International Classification of Diseases (ICD-11), the term chronic primary pain refers to pain that has no clear underlying cause and chronic secondary pain is used for pain associated with a recognised diagnosis or pathology [4]. CPP refers to persistent continuous or recurrent pain perceived in structures related to the male or female pelvis for ≥3 months, but a longer period of >6 months may be appropriate for cyclical pain.

Aetiology and Pathophysiology
Peripheral and Central Mechanisms
Animal and clinical research have indicated that many underlying chronic pain mechanisms are centrally mediated with central sensitisation and neural pathway modulation maintaining pain in the absence of an
on-going peripheral trigger or pathology [5]. Perception of a painful stimulus requires transmission of information to higher centres and activated pain pathways are modulated at the spinal cord level by ascending and descending pathways. Peripherally, acute pain mechanisms can lead to sensitisation of nociceptive transducers and activation of silent afferents that increase afferent signalling and maintain pain perception. Central sensitisation [6] is responsible for a decrease in response threshold and an increase in the magnitude and duration of dorsal horn neurone response. Increased signalling to the CNS amplifies what is perceived from a peripheral stimulus (hyperaesthesia) so that non-painful stimuli are perceived as painful (allodynia) and noxious stimuli are magnified with increased pain (hyperalgesia). In visceral hyperalgesia, sub-threshold non-perceptible visceral stimuli are perceived resulting in sensations that are often painful. Convergence of afferents from visceral and somatic pathways may result in pain being perceived at a different location to the site where the original stimulus causing the pain originates (referred pain) as higher centres fail to distinguish the source of the nociceptive signal.

Sensitisation of autonomic nervous system afferent fibres can cause a sensitivity to sympathetic stimulation and modification of the efferent output may produce end-organ dysfunction and functional abnormalities. Sensitisation of somatic efferent pathways may explain trophic changes found in somatic tissues. Central mechanisms are also important in the pathogenesis of muscle hyperalgesia with muscle tenderness and trigger points implicated as a source of pain.

Psychological Mechanisms

Pain processing is complex as nociceptive pathway activation is associated with emotional, cognitive, behavioural, and sexual responses that involve neural networks rather than distinct centres. Psychological processes affect supratentorial processing of pain, producing inhibition and facilitation of nociceptive signals, influencing their appraisal and interpretation, and modulating the response and experience of pain. Functional MRI has indicated that psychological modulation of visceral pain probably involves multiple pathways that result from a persistent strengthening of synapses (long-term potentiation) in response to patterns of activity [7]. Psychological factors are relevant to the maintenance of pelvic pain, as beliefs about pain contribute to its experience and symptom-related anxiety and central pain amplification may be measurably linked [8]. The various mechanisms of CNS facilitation, amplification, and failure of inhibition, mean that there is no simple relationship between physical findings, pain experienced and resulting distress and restriction of activities.

Risk Factors

Many factors can increase an individual’s susceptibility to developing chronic pain. Genetics play a role as family clusters of pain conditions have been reported with subtle changes in receptors and their transmitters [9]. Developmental, environmental, and social factors are important as twin studies have shown that the impact of genetics on the variation in individual susceptibility for some pain syndromes is low [10]. The endocrine system is important in visceral function and stress related to significant life events may alter development of the hypothalamic–pituitary–adrenal axis and the chemicals released [11]. Upregulation of corticotrophin-releasing hormone has been implicated in several pain states and may exert its effect by acting on mast cells. Stress can also influence pain levels through dysregulation of serotonergic pathways and evidence suggests that sex hormones may modulate nociception and pain [12].

Classification of CPP Syndromes

CPP conditions can be subdivided into pain syndromes (chronic primary pain) that have no obvious causative pathology and non-pain syndromes (chronic secondary pain) that have classical well-defined aetiology (e.g. infection, neoplasia). Pain syndromes are conditions in which pain is the main symptom and pain as a disease process is considered the cause.

Chronic primary pelvic pain syndromes (CPPPS) are a diagnosis of exclusion and refer to the occurrence of CPP when no proven infection or obvious local pathology is accounting for the pain. The term syndrome encompasses the negative emotional, cognitive, behavioural, sexual, and functional consequences of chronic pain and encourages a holistic approach to management with multidisciplinary input. In the absence of well-defined aetiological mechanisms, CPPPS are classified by describing them in terms of their symptoms, signs and, where possible, investigations. This phenotyping has clinical and research validity and should include disturbances of organ or system function caused by changes in their control mechanisms. Spurious terminology must be avoided, especially if it implies an unproven causality. Terms that end in ‘itis’ should only be used if infection and/or inflammation has been proven to be the cause of the pain.

Pain perception in CPPPS may focus on a particular pelvic organ/structure, may affect more than one pelvic organ, and can be associated with systemic disorders such as chronic fatigue syndrome and fibromyalgia. When pain is localised to a single organ, some specialists use specific end-organ terms (e.g. primary bladder pain syndrome [PBPS]). For non-specific, poorly localised pelvic pain affecting more than one
organ site, the generic term CPPPS should be applied. Despite a general tendency to move away from end-organ nomenclature, a diagnosis or name ascribed to a set of symptoms can provide patients with a sense of being understood, may help with acceptance of the problem as chronic, resolve unfounded fears about its implications, and encourage engagement with therapeutic endeavours and self-management.

**Prevalence**

Pelvic pain syndromes increase with age but information on their true prevalence is limited by variations in diagnostic criteria, evaluation tools, and symptom overlap with other conditions.

**Functional Disturbances**

**Sexual Dysfunction**

Studies of men with pelvic pain have reported higher chances of suffering from erectile and ejaculatory dysfunction [13]. Women with CPP have more sexual problems than patients with any other type of chronic pain disorder with sexual avoidance, dyspareunia, and ‘vaginismus’ most commonly reported [14]. Psychological factors (low self-esteem, depression, anxiety), physiological factors (such as fatigue, nausea, and pain) and pain medications (opioids, selective serotonin re-uptake inhibitors) can contribute to loss of libido and affect sexual function.

**Pelvic Floor Muscle Dysfunction**

An association between pelvic pain and muscular dysfunction (especially overactivity) is now recognised and has been reported in patients with CPP [15,16]. Repeated or chronic muscular overload can activate trigger points within the pelvic floor and adjacent (abdominal, gluteal, and iliopsoas) muscles. Trigger points are hyper-irritable spots within taut muscle bands that prevent full muscle lengthening and restrict range of movement. Pain is aggravated by trigger point pressure or sustained/repeated pelvic floor muscle contraction such as pain related to voiding or defecation.

**Clinical Assessment**

**History**

CPPPSs are symptomatic diagnoses so history is key in evaluating patients. Specific disease-associated pelvic pain must be ruled out and ‘red flag’ symptoms investigated by the relevant end-organ specialist. Some patients can relate pain onset to an acute event such as surgery, sepsis, or trauma, but for most it will be idiopathic. Burning is the commonest descriptor for neuropathic-type pain but crushing and electric are also used. Patients may report the feeling of a swelling or foreign body, such as a golf or tennis ball, in the rectum or perineum.

Enquiring about pelvic organ function is important for phenotyping a patient’s condition: lower urinary tract function and the influence of micturition on pain, anorectal function and the relationship between bowel habit and pain, sexual function, and gynaecological symptoms. In women, it is also important to assess for the presence of a temporal relation between pain and the menstrual cycle. A sexual history, including previous sexually transmitted infections, urethral/vaginal discharge, previous sexual trauma, and a woman’s cervical smear history is mandatory. A full urogynaecological history is important in individuals who have had continence or prolapse surgery using non-absorbable mesh. Dysfunction affecting two or more pelvic organs, should raise suspicion of pelvic floor muscle dysfunction.

Determining disease severity, its progression, and treatment response requires validated symptom-scoring instruments. They are recommended for basic evaluation and therapeutic monitoring of patients with CPPPS. Where the primary treatment outcome is pain relief, it is useful to agree a clinically meaningful level of relief before starting treatment. The most reliable methods for assessing pain are a 5-point verbal scale (none, mild, moderate, severe, very severe pain), a visual analogue spatial scale or a 0–10 numerical scale. Generic QoL measures are important, and the Brief Pain Inventory provides a broad assessment of the impact of pain on various aspects of life [17]. In males, sexual dysfunction can be evaluated using the International Index of Erectile Function and Premature Ejaculation Diagnostic Tool. The Female Sexual Function Index (FSFI) is a brief, multi-dimensional self-report instrument developed for assessing key dimensions of sexual function in women including desire, subjective arousal, lubrication, orgasm, satisfaction, and pain.

Direct questioning about the patient’s view of what is wrong, and their concerns can be more helpful than anxiety questionnaires. Anxiety about pain often refers to fears about missed pathology (particularly cancer) [8] or uncertainties about treatment and prognosis. Depression or depressed mood are common in chronic pain [18], often due to losses (work, leisure activities, social relationships, etc.) related to chronic pain.

**Physical Evaluation**

Clinical examination (with a chaperone present) helps to confirm or refute initial impressions gained from the history. Appropriate consent must be obtained including the risk of exacerbating pain during examination. The approach to examination may need to be modified in light of a patient’s...
previous experiences. Abdominal and pelvic examination including the external genitalia aims to exclude gross pelvic pathology and demonstrate sites of tenderness. Neurological examination is considered an integral part of the assessment and undertaken if appropriate. Many authors recommend assessing for cutaneous allodynia along the dermatomes of the abdomen (T11–L1) and the perineum (S3) and recording the degree of tenderness. The bulbocavernosus reflex in men provides information about the intactness of the pudendal nerves. A general musculoskeletal (tender point) evaluation, including muscles outside the pelvis, may help diagnose myofascial aspects of pelvic pain [19].

When assessing pelvic floor muscle function, a vaginal or rectal examination should be performed according to the ICS report [20]. An internal examination is important for diagnosing pelvic organ prolapse and cervical abnormalities in women. Perianal dermatitis can be a sign of faecal incontinence or diarrhoea and anal fissures may be overlooked. DRE is used to assess anal sphincter tone, the rectum, muscle tenderness and trigger points (including puborectalis), and prostate abnormalities including pain on palpation.

Investigations

There is no specific diagnostic test for CPPPS. Investigations are used to identify and exclude specific diseases associated with pelvic pain and for phenotypic description of pain syndromes. Investigations should be performed according to appropriate guidelines to exclude diseases with known aetiologies that present with symptoms identical to those of CPPPS.

Phenotyping

Given the polysymptomatic nature of CPPPS, clinical phenotyping systems can aid and standardise assessment of affected individuals by setting out series of domains that should be considered. Clinical phenotyping systems promote holistic patient care and potentially simplify treatment by promoting goal-directed multimodal therapy. UPOINTS (a phenotyping system that evaluates urinary [U], psychosocial [P], organ-specific [O], infection [I], neurological/systemic [N], muscle tenderness [T], and sexological [S] domains) is a widely known system despite its possible under-assessment of relevant psychological variables (Fig. 1) [21]. Ensuring clear records for each affected domain will help support treatment.

Management

The management of CPPPS is based on a bio-psychosocial model with active patient involvement. Ensuring appropriate patient information and understanding improves treatment adherence and underpins self-management. Single interventions rarely work in isolation and multimodal interventions addressing affected domains need to be considered within a personalised management strategy. A general overview of available treatment options is outlined below, with CPPPS-specific management detailed in subsequent sections. Where no evidence-based treatments exist, CPPPS management should be underpinned by the principles that apply to other chronic pain disorders (Fig. 2).

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**Fig. 1 Phenotyping of pelvic pain UPOINTS system.**

<table>
<thead>
<tr>
<th>Phenotyping</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urinary</strong></td>
<td>Symptom questionnaire, bladder diary, uroflowmetry, ultrasound, cystoscopy</td>
</tr>
<tr>
<td><strong>Psychology</strong></td>
<td>Anxiety about pain, catastrophising, depression, history of negative sexual experiences</td>
</tr>
<tr>
<td><strong>Organ specific</strong></td>
<td>Ask about gynaecological, gastrointestinal, ano-rectal complaints, Gynaecological examination, rectal examination</td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td>Urine culture, semen culture, vaginal swabs, stool culture</td>
</tr>
<tr>
<td><strong>Neurological</strong></td>
<td>Ask about neurological symptoms (sensory loss, dysaesthesia), Neurological examination: sensory problems, sacral reflexes, muscular function</td>
</tr>
<tr>
<td><strong>Tender muscle</strong></td>
<td>Palpation of pelvic floor muscles, abdominal muscles and glutal muscles</td>
</tr>
<tr>
<td><strong>Sexological</strong></td>
<td>Erectile and ejaculatory function, arousal, lubrication, post-orgasm pain</td>
</tr>
</tbody>
</table>
Physical Therapy

Patients with CPP often have pelvic floor muscle dysfunction [22] and pelvic floor re-education helps regain normal function. Pelvic floor relaxation techniques taught by specialised physiotherapists can reduce pelvic floor over-activity and help interrupt the pain-spasm cycle. Myofascial trigger points can be treated by manual therapy and dry or wet needling, but strong evidence for effectiveness of these techniques is lacking [23,24]. Encouraging chronic primary pain sufferers to remain physically active has general health benefits, but exercise has been shown to reduce pain and improve QoL especially for professionally-led supervised group exercise [25].

Psychological Therapy

Early identification and management of psychological symptoms such depression and anxiety may ameliorate pain and reduce distress. Psychological interventions can be directed at the pain itself to reduce its impact on life or at adjustment to pain to improve mood, function and reduce healthcare use, with or without pain reduction [26]. A systematic review of the few heterogeneous trials of psychologically-based treatment for pelvic pain found some short-term benefits for pain comparable to that achieved by pharmacotherapy, but this was not sustained at follow-up.

Pharmacological Treatment

Few studies have investigated medications used for CPPPS [27], so the evidence for pharmacotherapy is derived from findings for general chronic pain. If drug benefit is limited by side-effects, then dose titration is used to determine the lowest effective dose.

Simple Analgesia

Paracetamol is an antipyretic analgesic with a central mechanism of action that is well tolerated with few side-effects [28]. NSAIDs are anti-inflammatory, antipyretic analgesics that act peripherally by inhibiting the enzyme cyclooxygenase. NSAIDs have a higher incidence of side-effects and evidence is lacking for their use in CPP.

Neuromodulators

Neuromodulators are used to modulate neuropathic or centrally mediated pain. The evidence for treatment of CPP is lacking but is present for other painful conditions. Several classes are available, but all have side-effects that limit use. The UK National Institute for Health and Clinical Excellence has reviewed the pharmacological management of
neuropathic pain with recent guidance on neuromodulator use in chronic pain [25,29].

Despite being an off-label indication, several antidepressants have been recommended for treating chronic primary pain. Tricyclic antidepressants have anxiolytic effects with multiple mechanisms of action including acetylcholine receptor blockade, inhibition of serotonin and noradrenaline re-uptake, and blockade of H1 histamine receptors. Amitriptyline is most commonly used with doses ranging from 10 to 150 mg/day, but nortriptyline and imipramine are alternatives. Duloxetine is the only licensed serotonin-noradrenaline re-uptake inhibitor antidepressant with evidence for use in neuropathic pain. There is moderately strong evidence of benefit in diabetic neuropathy and fibromyalgia at a dose of 60 mg/day, but side-effects often limit use [30]. The anticonvulsant carbamazepine has evidence of moderate benefit for neuropathic pain but is no longer a first-choice agent because of potentially serious side-effects [31]. Other anticonvulsants used for neuropathic pain include gabapentin and pregabalin, but the evidence for use in primary pelvic pain is limited with at least one publication suggesting gabapentin does not help [32]. Consequently, anticonvulsants are best administered by pain specialists familiar with their use.

**Opioids**

Although opioids may be beneficial in chronic non-cancer pain in small numbers of patients at low doses in a managed setting, there is mounting evidence of a limited role in this population. Opioids can have harmful effects on the endocrine and immune systems with a growing understanding of opioid-induced hyperalgesia, in which patients taking opioids paradoxically, become more sensitive to painful stimuli [33]. Side-effects are common, including constipation, nausea, voiding dysfunction, opioid tolerance, and psychological changes, with the risk of harm increasing substantially at doses ≥120 mg/day morphine equivalence. Opioids should be administered by clinicians experienced in their use with arrangements made for formal monitoring, follow-up, and review. ‘Opioids Aware’ is an excellent web-based resource for patients and healthcare professionals (https://fpm.ac.uk/opioids-aware) [33].

**Cannabinoids**

The evidence base for cannabinoid use in pain is weak and well-conducted trials are necessary [34].

**Nerve Blocks**

Nerve blocks may have a diagnostic and therapeutic role for pain management, but the evidence base for these interventions for chronic non-malignant pain is weak [35]. Injection of local anaesthetic and steroid at a nerve injury site may produce therapeutic actions by blocking sodium channels and reducing inflammation and swelling.

**Urological Pain Syndromes**

**Primary Prostate Pain Syndrome (PPPS)**

PPPS refers to persistent or recurrent episodic pain perceived in the prostate for ≥3 months with no proven infection or obvious local pathology. The terms chronic prostatitis and prostatodynia should be avoided. No single aetiological explanation has been identified and PPPS probably develops in susceptible men exposed to unidentified initiating factors. Infection should be excluded with microscopy and culture of voided urine pre- and post-prostate massage (two-glass test) being a useful bacterial localisation screening procedure [36]. In high-risk men, PSA testing and MRI scanning may be considered after appropriate counselling. The National Institute of Health consensus classification of prostatitis includes infection (types I and II), which are best considered as specific disease-associated pelvic pain [37]. The National Institute of Health Chronic Prostatitis Symptom index is a validated symptom-scoring tool. See Table 1 for a summary of the management options for PPPS.

**Primary Bladder Pain Syndrome**

PBPS refers to persistent or recurrent pain perceived supraperically in the bladder area, accompanied by at least one other symptom, such as worsening pain with filling, transient relief with voiding, and daytime and/or night-time urinary frequency. Terms such as interstitial cystitis (IC) and painful bladder syndrome are no longer recommended.

The cause is thought to be an initial unidentified bladder insult leading to urothelial damage, neurogenic inflammation, and pain. An infective cause has not been confirmed. Defects in the urothelial glycosaminoglycan layer have been implicated with a role for mast cell histamine release proposed. PBPS prevalence ranges from 0.06% to 30% with a female predominance (about 10:1) [38,39] but no clear racial difference [40]. There is increasing evidence that children can be affected [41].

Urinary analysis and urine culture (including culture for tuberculosis if sterile pyuria) should be checked with urine cytology also recommended in high-risk groups. Pain in PBPS does not correlate with cystoscopic or histological findings, but these are important for diagnosis, ruling out confusable conditions and defining phenotypes. The European Society for the Study of Interstitial Cystitis (ESSIC) has suggested a standardised scheme of sub-classifications [42] to acknowledge differences and make it easier to compare.
various studies (Table 2). The O’Leary-Sant Symptom Index (Interstitial Cystitis Symptom Index) is a symptom-scoring instrument validated in a large study [43]. Botulinum toxin injections, neuromodulation, and transurethral resection of Hunner lesions have been shown to be effective in subsets of patients. Intravesical therapies and surgical intervention should be considered when conservative approaches fail. See Table 3 for a summary of the management options for PBPS.

Primary Scrotal Pain Syndrome

Primary scrotal pain syndrome refers to persistent or recurrent episodic pain perceived within the contents of the scrotum. No specific pathology is identifiable, but an injury or intervention along the course of the ilioinguinal, genitofemoral and pudendal nerves that innervate the scrotum can cause pain perceived in that area. Urinary tract and sexually transmitted infections need to be excluded. Scrotal ultrasonography does not help in diagnosis or treatment of scrotal pain but excludes confusable conditions. Microsurgical denervation of the spermatic cord can be considered in patients who have failed conservative and pharmacological treatment, as it can provide good long-term symptomatic relief in patients with testicular pain responding to spermatic cord nerve block [44].

Primary Urethral Pain Syndrome

Primary urethral pain syndrome can affect men and women and refers to chronic or recurrent episodic pain perceived in the urethra. As with PBPS, epithelial damage and neuropathic hypersensitivity following UTI are thought to be important. There is no specific treatment, but laser therapy of the trigone has been reported with good results [45].

Non-Urological Pain Syndromes

Primary Vulvar Pain Syndrome (PVPS)

PVPS refers to pain in the vagina or female external genital organs that persists for >3 months and can be generalised or focal. The terms vulvodynia and chronic vaginal pain are no longer recommended. In generalised PVPS, pain occurs in different areas of the vulva at different times and may be constant or intermittent. Touch or pressure does not initiate

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Management options for PPPS.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td><strong>Comment</strong></td>
</tr>
<tr>
<td>Alpha blockers</td>
<td>Moderate treatment effect if PPPS duration &lt;12 months</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>Use quinolones or tetracyclines for minimum of 6 weeks in treatment naïve patients</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Moderate treatment effect. Side-effects from long term use should be considered</td>
</tr>
<tr>
<td>Phytotherapy</td>
<td>Beneficial effect on pain and overall favourable treatment response</td>
</tr>
<tr>
<td>Pentosan polysulphate</td>
<td>Limited evidence for high-dose oral pentosan polysulphate</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Evidence for lack of effectiveness</td>
</tr>
<tr>
<td>Muscle relaxants</td>
<td>Insufficient data on effectiveness</td>
</tr>
<tr>
<td>Botulinum toxin A injection</td>
<td>Limited evidence for treatment effect in PPPS</td>
</tr>
<tr>
<td>Neuromodulation</td>
<td>Posterior tibial nerve stimulation probably effective in PPPS</td>
</tr>
<tr>
<td>Physical therapy</td>
<td>Acupuncture is superior to sham acupuncture in improving symptoms and QoL</td>
</tr>
<tr>
<td>Surgery</td>
<td>No evidence for surgical management</td>
</tr>
</tbody>
</table>

See EAU guidelines for more details.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>ESSIC classification of PBPS types according to results of cystoscopy with hydrodistension and biopsies [1].</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biopsy</strong></td>
<td><strong>Cystoscopy with hydrodistension</strong></td>
</tr>
<tr>
<td>Not done</td>
<td>XX</td>
</tr>
<tr>
<td>Normal</td>
<td>XA</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>XB</td>
</tr>
<tr>
<td>Positive</td>
<td>XC</td>
</tr>
</tbody>
</table>

**Symbol 1 – Cystoscopic findings**

| X – not done | 1 – normal | 2 – glomerulations Grade II or III | 3 – Hunner’s lesion per Fall’s definition with or without glomerulations |
| X – not done | A – normal | B – inconclusive | C – Histology showing inflammatory infiltrates and/or detrusor mastocytosis and/or granulation tissue and/or intrafascicular fibrosis |

For example, type 1B refers to a patient with a normal cystoscopy and inconclusive biopsy results.
Table 3 Management options for PBPS.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lifestyle</strong></td>
<td>Avoidance of certain foods and drink may reduce symptoms</td>
</tr>
<tr>
<td><strong>Neuromodulators</strong></td>
<td>Amitriptyline is effective for pain and related symptoms</td>
</tr>
<tr>
<td>Pentosan polysulphate</td>
<td>Oral treatment is effective for pain and related symptoms</td>
</tr>
<tr>
<td>Intravesical treatment</td>
<td>Oral treatment may be enhanced by intravesical pentosan polysulphate</td>
</tr>
<tr>
<td></td>
<td>Intravesical lidocaine plus sodium bicarbonate is effective in the short term</td>
</tr>
<tr>
<td><strong>Neuromodulation</strong></td>
<td>Sacral neuromodulation may be effective in PBPS</td>
</tr>
<tr>
<td>Botulinum toxin A injection</td>
<td>Pudendal nerve stimulation is superior to sacral nerve modulation</td>
</tr>
<tr>
<td>Surgery</td>
<td>Limited evidence for benefit</td>
</tr>
<tr>
<td></td>
<td>Consider botulinum toxin injections if intravesical instillation therapies have failed</td>
</tr>
<tr>
<td></td>
<td>Transurethral resection/fulguration may be effective in PBPS type 3 C</td>
</tr>
<tr>
<td></td>
<td>Major surgery is last resort – if considered, it should be undertaken</td>
</tr>
<tr>
<td></td>
<td>in a specialist centre with a multidisciplinary team approach</td>
</tr>
</tbody>
</table>

See EAU guidelines for more details.

it but can exacerbate it. In focal PVPS, the pain is at the vaginal introitus and described as a burning sensation that only develops after touch or pressure, such as during penetration.

Primary Anorectal Pain Syndrome (PAPS)

PAPS refers to continuous, recurrent, or episodic pain perceived in the anal canal and/or rectum in the absence of proven infection or local pathology. The Rome III criteria for functional anorectal pain disorders should be fulfilled for 3 months with symptom onset ≥6 months before diagnosis [46]. Pain may be continuous (chronic proctalgia) or intermittent with episodic cramping, aching, or stabbing pain lasting several seconds to 30 min with no pain between episodes (proctalgia fugax). Most patients with intermittent PAPS do not report it to their physicians with pain attacks occurring less than five times a year in over half of patients. Bowel dysfunction is common with excessive straining, anal digitation in dyssynergic (paradoxical) defecation and a sensation of anal blockage reported by some affected individuals. During examination, exquisite tenderness during posterior traction on the puborectalis muscle (‘levator ani syndrome’) is thought to be due to pelvic floor muscle over-activity.

Chronic Post-Surgical Pain (CPSP)

CPSP is defined as pain that develops or increases in intensity after a surgical procedure and persists beyond the healing process (>3 months). It has now been classified by ICD-11 as a chronic pain condition. Abdominopelvic operations with higher risk of CPSP include bariatric surgery, inguinal hernia repair, vasectomy, hysterectomy, and caesarean section.

Post-vasectomy scrotal pain syndrome occurs in 2–20% of men who have undergone a vasectomy [47]. Underlying mechanisms are poorly understood, but the risk is significantly lower with the no-scalpel technique [48]. Reversal of vasectomy can cure symptoms especially if patency is achieved. A randomised controlled trial reported high rates of symptomatic improvement (80%) with pulsed radio-frequency to the ilioinguinal and genitofemoral nerves but follow-up was limited to 3 months. The evidence for epididymectomy is poor and is less likely to provide benefit if the epididymis has a normal sonographic appearance.

Post-inguinal hernia repair pain develops in up to 10% of patients at 6 months and may present with groin or scrotal pain. The risk is higher following laparoscopic rather than open surgery [49]. Limited evidence from case series has shown that neurectomy of damaged nerves can lead to symptomatic improvement.

The incidence of CPSP after hysterectomy is difficult to determine as pain is a common indication for the operation. Rates approximate 28%, so careful case selection and management of patient expectation is important [50]. There is also a significant incidence of CPSP at 12 months after caesarean section, so careful counselling is needed in non-emergency cases.

Flexible polypropylene plastic mesh implants developed and used to treat urinary stress incontinence and uroterovaginal prolapse now carry a significant ‘health and safety warning’ with complication rates close to 10% that include CPP, chronic infections, erosion into surrounding structures (vagina, bladder, and urethra) and nerve and musculoskeletal damage [51,52]. Mesh-related complications have a significant impact on patients’ QoL, so early recognition is important. Mesh removal may be necessary for difficult-to-treat pain and should be provided within multidisciplinary tertiary settings [53]. This is complex surgery requiring removal of dense scar tissue and reconstruction of the vagina, urethra, and bladder, but can have beneficial and durable effects on chronic pain [54].
Conclusions

CPPSSs are symptomatic diagnoses that have a significant negative impact on affected individuals. Specific disease-associated causes of pelvic pain need to be excluded. Phenotyping is important for diagnosis and provides an approach to management of affected patients by promoting goal-directed treatment of the functional, emotional, behavioural, sexual, and physical consequences. Evidence-based treatments for CPPSSs are limited, so management follows the principles used for treating other chronic pain disorders.

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Conflict of Interest

Daniel Engeler has previously received honoraria from Astellas Pharma, Janssen-Cillag and Medtronic. All other authors have no disclosure of interests to declare.

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Abbreviations: CPP, chronic pelvic pain; CPPPS, chronic primary pelvic pain syndrome; CPSP, chronic post-surgical pain; EAU, European Association of Urology; ESSIC, European Society for the Study of Interstitial Cystitis; FSFI, Female Sexual Function Index; ICD-11, WHO International Classification of Diseases 11th Revision; PAPS, primary anorectal pain syndrome; PBPS, primary bladder pain syndrome; PPBS, primary prostate pain syndrome; PVPS, primary vulvar pain syndrome; QoL, quality of life.